NEWSLETTER

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#### **BIBLIOGRAFIA ADHD MARZO 2014**

#### ADHD Atten Deficit Hyperact Disord. 2014;6:19-23.

EVIDENCE OF ASSOCIATION BETWEEN SNAP25 GENE AND ATTENTION DEFICIT HYPERACTIVITY DISORDER IN A LATIN AMERICAN SAMPLE.

#### Galvez JM, Forero DA, Fonseca DJ, et al.

Attention deficit hyperactivity disorder (ADHD) is one of the most highly heritable behavioral disorders in childhood, with heritability estimates between 60 and 90 %. Family, twin and adoption studies have indicated a strong genetic component in the susceptibility to ADHD. The synaptosomal-associated protein of molecular weight 25 kDa (SNAP25) is a plasma membrane protein known to be involved in synaptic and neural plasticity. Animal model studies have shown that SNAP25 gene is responsible for hyperkinetic behavior in the coloboma mouse. In recent studies, several authors reported an association between SNAP25 and ADHD. In this study, we used a case-control approach to analyze the possible association of two polymorphisms of SNAP25 for possible association with ADHD in a sample of 73 cases and 152 controls in a Colombian children population. Polymorphisms are located in 3' untranslated region of SNAP25, positions T1065G and T1069C. We found a significant association with the GT haplotype (rs3746554{pipe}rs1051312) of SNAP25 (p = 0.001). Evidence of association was also found for the G/G genotype of rs3746554 (p = 0.002) and C/C genotype of rs1051312 (p = 0.009). This is the first study in a Latin American population. Similar to other studies, we found evidence of the association of SNAP25 and ADHD.

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#### ADHD Atten Deficit Hyperact Disord. 2014. THE IMPACT OF ADHD ON MORALITY DEVELOPMENT. Groman CMJ, Barzman DH.

attachment will serve to validate this claim.

# Attention deficit hyperactive disorder (ADHD) is one of the most commonly diagnosed childhood mental disorders. This pervasive disorder can affect all aspects of the child's life, including, but not limited to: peer relations, adult relations and intellectual development. As a direct result of ADHD, many of these deficiencies pervade through the child's life into adulthood. Although there is a growing number of literature focusing on the sequela of ADHD, especially social deviance, most of the literature's scope is limited to the connection between ADHD and criminality. This finite perspective provides little insight into the developmental characteristics which actually link ADHD to criminality. The most glaring example of an obscured developmental link is that of moral judgment. The following is an attempt to draw a meaningful connection between deficient moral development and ADHD, especially as it relates to attachment theory. Connecting previous research relevant to the topic as well as time-tested psychological theories on morality and

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Per la ricerca degli articoli pubblicati nella letteratura scientifica nel mese in esame sono state consultate le banche dati

Medline, Embase, PsycINFO e PsycArticle utilizzando le seguenti parole chiave (o i loro sinonimi): 'Attention deficit disorder', 'Attention deficit hyperactivity disorder', 'Infant', 'Child', 'Adolescent', 'Human'. Sono qui riportate le referenze considerate rilevanti e pertinenti.

ADHD Atten Deficit Hyperact Disord. 2014;1-6.

## IS HIGH PREVALENCE OF VITAMIN D DEFICIENCY A CORRELATE FOR ATTENTION DEFICIT HYPERACTIVITY DISORDER?

#### Kamal M, Bener A, Ehlayel MS.

The aim of the study was to determine the association between vitamin D and attention deficit hyperactivity disorder (ADHD), and difference in the level of vitamin D in ADHD children and control. This a case-control study carried out in school health and primary health care clinics. A total of 1,331 children and adolescents who were diagnosed with ADHD based on clinical criteria and standardized questionnaires were enrolled in this study and were matched with 1,331 controls, aged 5-18 years old. Data on body mass index (BMI), clinical biochemistry variables including serum 25-hydroxyvitamin D were collected. The study found significant association between ADHD and vitamin D deficiency after adjusting for BMI and sex (adj. OR 1.54; 95% CI 1.32-1.81; P<0.001). Majority of the ADHD children were in the age group 5-10 years (40.7%), followed by 11-13 years (38.4 %). The proportion of BMI <85th percentile was significantly over represented in ADHD group as compared to healthy control (87.8 vs. 83 %; P<0.001, respectively), while on the other hand, BMI >95th percentile was over represented in the control than ADHD group (7.6 vs. 4.6 %; P < 0.001, respectively). Mean values of vitamin D (ng/mL) were significantly lower in ADHD children (16.6 (plus or minus) 7.8) than in healthy children (23.5 (plus or minus) 9.0) (P<0.001). There was significant correlation between vitamin D deficiency and age (r=-0.191, P=0.001); calcium (r=0.272, P=0.001); phosphorous (r=0.284, P=0.001); magnesium (r=0.292, P=0.001); and BMI (r=0.498, P=0.001) in ADHD children. The vitamin D deficiency was higher in ADHD children compared to healthy children.

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#### ADHD Atten Deficit Hyperact Disord. 2014;1-8.

# A PROSPECTIVE LOOK AT SUBSTANCE USE AND CRIMINAL BEHAVIOR IN URBAN ADHD YOUTH: WHAT IS THE ROLE OF MALTREATMENT HISTORY ON OUTCOME?

#### De Sanctis VA, Newcorn JH, Halperin JM.

Children with attention-deficit/hyperactivity disorder (ADHD) are at heightened risk of antisocial behavior during adolescence/early adulthood. Here, we characterize the antisocial outcomes of a sample of urban, lower-socioeconomic-status, ethnically diverse ADHD youth and investigate the impact of maltreatment history on criminal and substance use disorder (SUD) outcomes. Ninetyeight participants diagnosed with ADHD in childhood were re-assessed 10 years later and compared with controls. Regression analyses investigated the effect of maltreatment on antisocial outcomes among four groups based on ADHD and maltreatment status. ADHD subjects and controls did not differ in rates of arrest, conviction, incarceration, or recidivism. ADHD youth were younger at their first arrest with higher rates of SUDs when compared to controls. Controls and ADHD subjects with maltreatment had significantly higher rates of SUDs compared to the no-ADHD/no-maltreatment group. Only ADHD youth with maltreatment had significantly higher rates of arrest than the reference group. In contrast to prior studies, ADHD youth did not differ from controls on most measures of antisocial behavior. Maltreatment increased the rate of arrest only among ADHD youth, though increased the rate of SUD for ADHD youth and controls. This suggests that ADHD youth, in the absence of maltreatment, are at no greater risk of SUDs or arrest than controls without maltreatment.

ADHD Atten Deficit Hyperact Disord. 2014;6:25-34.

#### PROGNOSTIC FACTORS OF IMPROVEMENT IN HEALTH-RELATED QUALITY OF LIFE IN ATOMOXETINE-TREATED CHILDREN AND ADOLESCENTS WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER, BASED ON A POOLED ANALYSIS.

#### Montoya A, Quail D, Anand E, et al.

The objective of this study is to identify prognostic factors of treatment response to atomoxetine in improvement of health-related quality of life (HR-QoL), measured by the Child Health and Illness Profile-Child Edition Parent Report Form (CHIP-CE PRF) Achievement and Risk Avoidance domains, in children and adolescents with attention-deficit/hyperactivity disorder (ADHD). Pooled data from 3 placebo-controlled trials and separate data from 3 open-label trials of atomoxetine in children and adolescents with ADHD were analyzed using logistic regression methods. Based on baseline impairment in the Achievement and/or Risk Avoidance domains (CHIP-CE PRF < 40 points), 2 subsamples of subjects were included. Treatment outcome was categorized as <5 points or (greater-than or equal to)5 points increase in the CHIP-CE PRF Achievement and Risk Avoidance domains. Data of 190 and 183 subjects from the pooled sample, and 422 and 355 subjects from the open-label trials were included in the analysis of Achievement and Risk Avoidance domains. Baseline CHIP-CE subdomain scores proved to be the most robust prognostic factors for treatment outcome in both domains, based on data from the pooled sample of double-blind studies and from the individual open-label studies (odds ratios [OR] 0.74-1.56, p<0.05; OR<1, indicating a worse baseline score associated with worse odds of responding). Initial treatment response ((greater-than or equal to)25 % reduction in ADHD Rating Scale scores in the first 4-6 weeks) was another robust prognostic factor, based on data from the open-label studies (OR 2.99-6.19, p<0.05). Baseline impairment in HR-QoL and initial treatment response can be early prognostic factors of atomoxetine treatment outcome in HR-QoL in children and adolescents with ADHD.

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#### ADHD Atten Deficit Hyperact Disord. 2014;6:1-10.

# EXECUTIVE FUNCTIONING IN ATTENTION-DEFICIT/HYPERACTIVITY DISORDER: QUESTIONING THE NOTION OF PLANNING DEFICITS WITH HEART RATE REACTIVITY.

#### Perrin PB, Case KH, Byrd DL, et al.

This study employed a paired stimulus paradigm to compare phasic changes in heart rate among children (age categories 6-8, 9-10, and 11-12) and adults (age categories 18-19 and 20-22) with attention-deficit/hyperactivity disorder (ADHD) and age-matched controls. A sample of 95 participants (19 ADHD-diagnosed children, 34 controls, 20 ADHD-diagnosed adults, and 22 controls) solved a planning task, the Tower of London, through 4 levels of difficulty. It was hypothesized that groups with ADHD would show greater heart rate acceleration and less final deceleration than would controls, and that these heart rate responses would change with age and difficulty level as well. Though heart rate differences were found among age categories and difficulty levels, none were found between participants with ADHD and controls. The lack of ADHD differences are not consistent with the behavioral evidence that planning by itself is one of the marked executive function deficits in ADHD. Because ADHD differences were not evident, the effects either were not present or were smaller than that of difficulty level and age. Possible explanations for this lack of difference and future directions are discussed.

#### Ann Med -Psychol. 2014.

# **ADHD:** THE RELEVANCE OF ASSOCIATING PHARMACOTHERAPY AND PSYCHODYNAMIC PSYCHOTHERAPY?

#### Adrian V.

Interest in attention deficit disorder/attention deficit hyperactivity disorder (ADD/ADHD) is growing, as evidenced by the number of scientific publications on the topic, as well as by the number of requests for child psychiatric consultations to diagnose ADD. The current clinical consensus is the result of the long evolution of a historical dichotomy between advocates for an organogenetic or psychopathological etiology of the disorder. Today, we question whether a "double reading" is possible taking into consideration both neuro-developmental factors as well as psychopathological elements? The contribution of complexity theorists and developmental phenomenology could help to conceptualize the ADD/ADHD as a complex and multifactorial disorder, which would support a "transversal" therapeutic approach involving psychoanalytical and psychopharmacology. However, questions remain regarding the effectiveness of psychoanalytical therapy and its association with pharmacotherapy in treating ADHD - and there appears to be little evidence of its effectiveness in existing literature. Thus, the possibility of a future therapeutic consensus for ADHD could be expected.

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#### Ann Biomed Eng. 2013;41:1968-78.

A DEVICE FOR CONTINUOUS MONITORING OF TRUE CENTRAL FIXATION BASED ON FOVEAL BIREFRINGENCE.

#### Gramatikov B, Irsch K, Mullenbroich M, et al.

A device for continuous monitoring of central fixation utilizes birefringence, the property of the Henle fibers surrounding the human fovea, to change the polarization state of light. A circular scan of retinal birefringence, where the scanning circle encompasses the fovea, allows identification of true central fixation - an assessment much needed in various applications in ophthalmology, psychology, and psychiatry. The device allows continuous monitoring for central fixation over an extended period of time in the presence of fixation targets and distracting stimuli, which may be helpful in detecting attention deficit hyperactivity disorder, autism spectrum disorders, and other disorders characterized by changes in the subject's ability to maintain fixation. A proof-of-concept has been obtained in a small study of ADHD patients and normal control subjects.

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Asia-Pacific Psychiatry. 2014;6:71-76.

IMPACT OF ATTENTION DEFICIT HYPERACTIVITY DISORDER-LIKE SYMPTOMS ON THE CLINICAL FEATURES OF ADOLESCENTS WITH PERVASIVE DEVELOPMENTAL DISORDERS.

#### Suzumura S.

**Introduction**: Attention Deficit Hyperactivity Disorder (ADHD)-like symptoms are common among children and adolescents with Pervasive Developmental Disorders (PDD). The purpose of this study was to assess the impact of ADHD-like symptoms on the clinical features of adolescents with PDD.

**Methods**: A total of 72 subjects (between the ages of 12 and 17) diagnosed as having PDD were split into higher (ADHD+) and lower (ADHD-) groups according to the presence of ADHD-like symptoms as assessed with the Japanese version of the ADHD Rating Scale-IV (ADHD-RS-IV-J). Group differences in coexisting psychopathology, as assessed by the eight subscales of the

Japanese version of the Child Behavior Checklist for Ages 4-18 (CBCL/4-18-J) and autistic core features, as assessed by the adolescent part of the PDD-Autism Society of Japan Rating Scale (PARS), were examined.

**Results**: The ADHD+subjects showed a significantly higher degree of general psychopathology, including both externalizing and internalizing symptoms, as compared to subjects in the ADHD-subgroup. Additionally, the ADHD+subgroup showed greater impairment according to PARS scores.

**Discussion**: These results indicate an important role of ADHD-like symptoms in PDD. Therefore, parents/caregivers may find it useful to know to what extent their child's ADHD-like symptoms deviate from the norm for PDD adolescents and the implications of these symptoms for long-term care. In addition, clinicians would be well advised to consider further systematic assessment of ADHD-like symptoms.

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#### BJOG Int J Obstet Gynaecol. 2014.

# ATTENTION DEFICIT HYPERACTIVITY DISORDER AND AUTISM SPECTRUM DISORDER IN CHILDREN BORN TO MOTHERS WITH THYROID DYSFUNCTION: A DANISH NATIONWIDE COHORT STUDY.

#### Andersen S, Laurberg P, Wu C, et al.

**Objective**: To examine the association between maternal hyper- and hypothyroidism and the risk of attention deficit hyperactivity disorder (ADHD) and autism spectrum disorder (ASD) in the child. **Design**: A population-based cohort study.

Setting: Singletons liveborn in Denmark between 1991 and 2004.

**Population**: A total of 857 014 singletons alive and living in Denmark at the age of 3 years.

**Methods**: Information on the diagnosis and/or treatment of maternal thyroid disease and the neurodevelopmental disorders ADHD and ASD in the child was obtained from Danish nationwide registers. The Cox proportional hazards model was used to estimate the hazard ratio (HR) with 95% confidence interval (95% CI) for risk of ADHD and ASD in children born to mothers with thyroid dysfunction, adjusting for potential confounding factors.

Main outcome measures: ADHD and ASD in the child.

**Results**: Altogether, 30 295 singletons (3.5%) were born to mothers with thyroid dysfunction. Maternal hyperthyroidism diagnosed and treated for the first time after the birth of the child increased the risk of ADHD in the child (adjusted HR 1.23; 95% CI 1.05-1.44), whereas hypothyroidism increased the risk of ASD (adjusted HR 1.34; 95% CI 1.14-1.59). No significant association was seen for maternal diagnosis and treatment prior to the birth of the child.

**Conclusions**: Children born to mothers diagnosed and treated for the first time for thyroid dysfunction after their birth may have been exposed to abnormal levels of maternal thyroid hormone already present during the pregnancy, and this untreated condition could increase the risk of specific neurodevelopmental disorders in the child.

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BMJ Open. 2014;4.

BEHAVIOURAL SLEEP PROBLEMS IN CHILDREN WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER (ADHD): PROTOCOL FOR A PROSPECTIVE COHORT STUDY.

#### Lycett K, Sciberras E, Mensah FK, et al.

**Introduction**: Children with attention-deficit/hyperactivity disorder (ADHD) commonly experience behavioural sleep problems, yet these difficulties are not routinely assessed and managed in this group. Presenting with similar symptoms to ADHD itself, sleep problems are complex in children

with ADHD and their aetiology is likely to be multifactorial. Common internalising and externalising comorbidities have been associated with sleep problems in children with ADHD; however, this relationship is yet to be fully elucidated. Furthermore, limited longitudinal data exist on sleep problems in children with ADHD, thus their persistence and impact remain unknown.

In a diverse sample of children with ADHD, this study **aims to**: (1) quantify the relationship between sleep problems and internalising and externalising comorbidities; (2) examine sleep problem trajectories and risk factors; and (3) examine the longitudinal associations between sleep problems and child and family functioning over a 12-month period.

**Methods and analysis**: A prospective cohort study of 400 children with ADHD (150 with no/mild sleep problems, 250 with moderate/severe sleep problems) recruited from paediatric practices across Victoria, Australia. The children's parents and teacher provide data at baseline and 6-month and 12-month post enrolment.

**Key measures**: Parent report of child's sleep problem severity (no, mild, moderate, severe); specific sleep domain scores assessed using the Child Sleep Habits Questionnaire; internalising and externalising comorbidities assessed by the Anxiety Disorders Interview Schedule for Children IV/Parent version.

**Analyses**: Multiple variable logistic and linear regression models examining the associations between key measures, adjusted for confounders identified a priori.

**Ethics and dissemination**: Ethics approval has been granted. Findings will contribute to our understanding of behavioural sleep problems in children with ADHD. Clinically, they could improve the assessment and management of sleep problems in this group. We will seek to publish in leading paediatric journals, present at conferences and inform Australian paediatricians through the Australian Paediatric Research Network.

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British Journal of Educational Psychology. 2014 Mar;84:86-107.

ACADEMIC BUOYANCY AND ACADEMIC OUTCOMES: TOWARDS A FURTHER UNDERSTANDING OF STUDENTS WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER (ADHD), STUDENTS WITHOUT ADHD, AND ACADEMIC BUOYANCY ITSELF.

#### Martin AJ.

**Background**: Academic buoyancy is students' capacity to successfully overcome setback and challenge that is typical of the ordinary course of everyday academic life. It may represent an important factor on the psycho-educational landscape assisting students who experience difficulties in school and schoolwork.

**Aims**: This study investigated the role of academic buoyancy in the achievement and cognitive, affective and behavioral engagement of (1) students with attention-deficit/hyperactivity disorder (ADHD) and (2) 'regular' (or 'general') students residing in the same classrooms and schools. The study also sought to extend prior research into academic buoyancy by including previously neglected and potentially influential factors such as personality and socio-economic status.

**Sample**: Participants were n=87 high school students with ADHD, n=3374 non-ADHD peers, and n=87 randomly drawn non-ADHD students. Method: Survey-based data were analyzed using multigroup (ADHD, non-ADHD, randomly weighted non-ADHD) multivariate (multiple independent/covariate and dependent variables) path analysis.

**Results**: The findings revealed a significant and positive association between academic buoyancy and outcomes for students with ADHD that generalized to non-ADHD groups. On occasion where academic buoyancy effects differed between the groups, effects favored students with ADHD. Furthermore, academic buoyancy explained significant variance in outcomes for both

groups of students after covariates (age, gender, parent education, language background, socioeconomic status, personality) were entered.

**Conclusion**: It is concluded that there is merit in widely promoting and fostering academic buoyancy among ADHD and non-ADHD students alike—and that academic buoyancy explains variance in outcomes beyond major intrapersonal factors such as personality, socio-economic status, ethnicity, and the like.

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Bulletin Clin Psychopharmacology. 2013;23:S80.

ATOMOXETINE AND METHYLPHENIDATE FOR THE TREATMENT OF ATTENTION DEFICIT HYPERACTIVITY DISORDER: A SIX-MONTH FOLLOW-UP STUDY.

#### Cetin FH, Taner YI, Torun YT, et al.

**Objective**: The aim of this study was to compare the efficacy and side effects of metylphenidate (MPH) and atomoxetine (ATX) for treatment of Attention Deficit Hyperactivity Disorder (ADHD).

**Method**: 147 patients between ages 7-16 years with ADHD and without other comorbid psychopathologies were included to the study. Out of 147, 98 patients completed the study. 32 patients used ATX and 66 patients used MPH in the study. Choice of medication was made randomly and patients were assessed at 1st,3rd and 6th month with Conners Teacher Rating Scale (CTRS) and clinic assessment. Efficay was defined as a decrease of 40% or more from baseline CTRS score at month 6. Side effects and safety were assessed at each visit by questionnaires.

**Results**: Medication groups had similar characteristics in terms of sociodemographic data and initial CTRS scores. Average drug doses were 0,68 mg/kg/day for MPH and 1,17 mg/kg/day for ATX. While efficacy rates in patients using MPH were 47% in hyperactivity symptom, 65,3% in attention deficit symptoms and 54,5% in conduct disorder symptoms; these rates were respectively 40,6%; 53,1% and 37,5% in patients using ATX. Side effect rates were 33,3% (n=22) in MPH group and 43,8% (n=14) in ATX group. There was no significant difference between the treatment groups in terms of efficacy and side effect rates (p>0.05). Also; there was no significant difference on CTRS scores between two medications as a function of time.

**Conclusion**: In this study, ATX and MPH were compared based on efficacy and side effects and no significant differences were found. Itnulls noteworthy that clinical improvement could be observed from first month with both of drugs. In summary, ATX and MPH had similar treatment profiles for ADHD.

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Bulletin Clin Psychopharmacology. 2013;23:S121-S122.

THE RELATIONSHIP BETWEEN SOLUBLE INTERCELLULAR ADHESION MOLECULES AND ATTENTION DEFICIT HYPERACTIVITY DISORDER.

#### Alasehirli B, Oguz E, Gokcen C, et al.

**Objective**: Attention deficit hyperactivity disorder (ADHD) is a common childhood-onset psychiatric disease, characterised by excessive overactivity, inattention and impulsiveness. It is suggested that prefrontal dopamine deficiency and central dopaminergic dysfunction could be the main factors for ADHD, but the mechanism of this deficiency and dysfunction and so the etiopathology of the disease is not fully understood. Although it is showed that inflammatory processes are involved in neurological and psychiatric disorders, such as depression and Parkinsonnulls disease, the studies for ADHD are very limited. In this study, we aimed to investigate whether there are associations between ADHD and changes in serum levels of serum

soluble intercellular adhesion molecules (s-ICAMs), which have an important role in inflammatory diseases. We also measured the levels of these molecules after treatment with oros-methylphenidate.

**Method**: Twenty-five patients diagnosed with ADHD according to DSM-IV-TR criteria and eighteen healthy volunteer controls were included in this study. The levels of sICAMs were measured in the serum of the patients and healthy volunteers by ELISA kit as described.

**Results**: The levels of ICAM-1 and ICAM-2 were significantly higher in patients compared with controls. The level of ICAM-1 was decreased in treated group, but this decrease was not significant. ICAM-2 levels decreased significantly after treatment by oros-methylphenidate compared with untreated group.

**Conclusion**: This is the first study pointing out the relationship between ICAM molecules and ADHD. ICAM-1 and 2, the molecules involved in inflammatory processes, are associated with ADHD. The changes in sICAM-2 level may have a therapeutic value in ADHD treatment.

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#### Bulletin Clin Psychopharmacology. 2013;23:S79.

## ASSOCIATION OF ADULT ADHD SUBTYPES AND RESPONSE TO METHYLPHENIDATE TREATMENT: A MRS STUDY.

#### Unal GA, Kenar ANI, Herken H, et al.

**Objective**: It is aimed to investigate the relation between adult ADHD (attention deficit hyperactivity disorder) subtypes and methylphenidate (MPH) treatment in adult ADHD patients and the changes in N-acetyl aspartate (NAA), creatine and choline levels in anterior cingulate cortex (ACC), cerebellum, striatum and dorsolateral prefrontal cortex (DLPFC) measured by magnetic resonance spectroscopy (MRS).

**Methods**: Sixty ADHD subjects were included into the study aging between 18 and 60 years. Levels of NAA, creatine and choline in ACC, cerebellum, striatum and DLPFC were measured with MRS. Then, 10 mg oral MPH was given to the subjects and the same metabolite levels were measured after an interval of 30 minutes.

**Results**: Distribution of the patients according to the ADHD subtypes was as follows: 21 of them (35,0%) were in the inattentive type, 11 of them (18,3%) were in the hyperactive type and 28 of them were (46,7%) in the combined type. NAA levels in striatum after MPH administration in the inattentive type were statistically higher than the ones in the hyperactive type. No difference was determined between the ADHD subtypes in terms of the changes of NAA levels in other brain areas. The difference between ADHD subtypes in terms of the changes of creatine and choline levels before and after MPH was not statistically significant. The decrease of creatine levels after MPH compared to the levels of creatine before MPH in ACC in the hyperactive type patients was statistically significant. The increase of choline levels after MPH compared to the levels of choline levels after MPH in cerebellum and striatum in the combined type patients were statistically significant.

**Conclusion**: Consequently, no clear association was found between ADHD subtypes and changes of brain metabolites with use of MPH in adult ADHD.

#### Bulletin Clin Psychopharmacology. 2013;23:S115.

# **M**ETHYLPHENIDATE TREATMENT IN A PATIENT WITH BIPOLAR DISORDER AND ATTENTION DEFICIT HYPERACTIVITY COMORBIDITY: A CASE REPORT.

#### Erdem M, Unlu G, Akarsu S.

Attention deficit hyperactivity disorder (ADHD) and mania show a broad overlap of symptoms and a high comorbidity. This situation moots questions about common neurobiological and pathological mechanisms and treatments. We report efficacy of additional methylphenidate treatment in a patient with bipolar disorder and ADHD comorbidity. A 32-year-old married man. He was admitted to outpatient clinic with complaints of inability to control his behaviors, inattention, hyperactivity and mood variability. His first psychiatric admission was ten years ago. He discontinued treatment because of lack of benefit. He had depressive episodes in 2006 and 2007, after than he was diagnosed with bipolar disorder. Mood stabilizer treatment was started in 2007. He experienced hypomanic and depressive episodes for 3-4 times, but he did not receive a regular treatment. In the mental examination at the time of hospitalization, his affect was observed as elevated and showed signs of mania. Young mania scale score was 10; Wender-Utah test result was compatible with the diagnosis. He was treated with valproic acid and quetiapine, initially. As he did not show improvement by means of attention deficits in the followup period, methylphenidate has been added on actual treatment. Patient has got significant benefit from treatment. Many symptoms of ADHD and mania share some pathogenetic routes. There is a consensus that stimulants should be used carefully in mania. This case indicated that stimulant can be use full in comorbid states and there is not much risk in the presence of mood stabilizers and close follow up.

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#### Cardiol Young. 2014;24:120-25.

# VENTRICULAR ARRHYTHMIAS IN CHILDREN WITH ATTENTION DEFICIT DISORDER-A SYMPTOM OF AUTONOMIC IMBALANCE?

#### Buchhorn R, Christian W.

**Objectives** Potential side effects of stimulants for attention deficit disorder are in the focus of scientific discussions, intensified by the higher number of prescriptions. Children with known arrhythmias or other severe cardiac problems should not receive stimulants because of their sympathomimetic effects.

**Methods** This is a retrospective analysis of 24-hour Holter electrocardiograms from 100 consecutive children with attention deficit disorder from January, 2006 to April, 2012.

**Results** In all, nine children had significant ventricular arrhythmia (mean age 11.4 (plus or minus) 3.1 years, 77% male, 77% received methylphenidate). All these children had ventricular parasystole-four of them with an accelerated idioventricular rhythm. A significant circadian rhythm of premature ventricular contractions in seven children and the effect of standing and exercise clearly indicate the influence of the autonomic nervous system. In these children, hourly analysis of circadian rhythm within a 24-hour period showed a highly significant correlation between premature ventricular contractions and the vagal tone indicated by the heart rate variability parameter RMSSD (r = -0.83; p < 0.001). Ventricular arrhythmia was unaffected in seven children in two children.

#### **NEWSLETTER – ADHD**

**Conclusion** By Holter electrocardiogram analysis, we observed a remarkably high incidence of ventricular parasystole and accelerated idioventricular rhythm in nine of 100 children with attention deficit disorder, which depends on autonomic imbalance and not on stimulant treatment.

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#### Cereb Cortex. 2014;24:935-44.

# FUNCTIONAL CONNECTIVITY OF SUBSTANTIA NIGRA AND VENTRAL TEGMENTAL AREA: MATURATION DURING ADOLESCENCE AND EFFECTS OF ADHD.

#### Tomasi D, Volkow ND.

Dopaminergic (DArgic) pathways play crucial roles in brain function and their disruption is implicated in various neuropsychiatric diseases. Here, we demonstrate in 402 healthy children/adolescents (12 (plus or minus) 3 years) and 704 healthy young adults (23 (plus or minus) 5 years) that the functional connectivity of DA pathways matures significantly from childhood to adulthood and is different for healthy children and children with attention-deficit/hyperactivity disorder (ADHD; N=203; 12 (plus or minus) 3 years). This transition is characterized by age-related increases in the functional connectivity of the ventral tegmental area (VTA) with limbic regions and with the default mode network and by decreases in the connectivity of the substantia nigra (SN) with motor and medial temporal cortices. The changes from a predominant influence of SN in childhood/adolescence to a combined influence of SN and VTA in young adulthood might explain the increased vulnerability to psychiatric disorders, such as ADHD, early in life. We also show that VTA and SN connectivity networks were highly reproducible, which highlights their potential value as biomarkers for evaluating DArgic dysfunction in neuropsychiatric disorders.

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#### Clin Case Stud. 2014;13:115-27.

PARENT-CHILD INTERACTION THERAPY WITH DEAF PARENTS AND THEIR HEARING CHILD: A CASE STUDY.

#### Armstrong K, David A, Goldberg K.

There are few proven effective treatments such as Parent-Child Interaction Therapy (PCIT) for use with deaf parents and their children, even though it is likely that the prevalence rate for disruptive behavior problems including attention deficit/hyperactivity disorder (ADHD) and oppositional defiant disorder (ODD) are similar to those reported for all U.S. children. Medication and behavioral therapy involving parents comprise the cornerstone for ADHD/ODD management, with PCIT endorsed as one of the most effective interventions available for children aged 2 to 7 years. This case study presents the implementation of PCIT with deaf parents and their 7-year-old hearing son with ADHD/ODD, with the help of a certified interpreter and readily available video technology. Findings from this case report documented PCIT as a promising treatment option for use with individuals who are deaf.

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Clin Neurophysiol. 2014;125:491-99.

**EEG** AND ELECTRODERMAL ACTIVITY IN GIRLS WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER. *Dupuy FE, Clarke AR, Barry RJ, et al.* 

**Objective**: This study investigated the Hypoarousal Model of Attention-Deficit/Hyperactivity Disorder (AD/HD) in girls.

**Methods**: 40 girls with AD/HD and 40 girl controls (aged 7-12. years) had an eyes-closed resting EEG recorded from 19 electrodes and Fourier transformed. Estimates for total power, absolute and relative power in the delta, theta, alpha, beta and gamma frequency bands, and theta/beta ratio were analysed in nine cortical regions. Skin conductance level (SCL) was simultaneously recorded. Regression analyses explored relationships between symptoms and physiology.

**Results**: Compared with controls, girls with AD/HD had globally elevated relative delta, globally reduced absolute beta, and globally reduced absolute and relative gamma activity. Girls with AD/HD also had lower mean SCL. Inattentive symptoms were predicted by elevated frontal relative delta, reduced SCL, and reduced temporal relative gamma activity, while elevated hyperactive-impulsive symptoms correlated with elevated frontal relative delta activity in both the patient and control groups.

**Conclusions**: These EEG results are comparable with the limited female AD/HD literature. Girls with AD/HD are hypoaroused, indicated by reduced SCL, and appear to have an anomalous arousal mechanism. Absolute and relative gamma results are similar to previous findings in AD/HD children. Symptom correlations with physiology offer intriguing insights for future research.

Significance: This is the first study to examine CNS arousal exclusively in girls with AD/HD.

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Curr Opin Ophthalmol. 2014 Mar;25:118-21.

#### ANESTHESIA CONSIDERATIONS IN PEDIATRIC GLAUCOMA MANAGEMENT.

#### Chang TC, Cavuoto KM.

**PURPOSE OF REVIEW**: This article reviews the potentially adverse neurodevelopmental effects of early exposure to general anesthesia and examines a changing paradigm in the management of pediatric glaucoma.

**RECENT FINDINGS**: Literature across multiple subspecialties has examined the potentially neurotoxic effects of general anesthesia on the developing child's brain. Associations between general anesthesia exposure early in life and attention deficit hyperactivity disorder, language processing, and cognition have been suggested but not confirmed. Several population studies support the conclusion that early anesthetic exposure may increase the risk of neurodevelopmental deficits, although this is unsupported in sibling cohorts. Newer technology such as rebound tonometry may decrease the frequency of examination under anesthesia in the long-term management of patients with pediatric glaucoma and may decrease the risk of these potentially adverse neurodevelopmental outcomes.

**SUMMARY**: As the potential long-term adverse neurodevelopmental effects of general anesthesia become better understood, pediatric glaucoma specialists should be cognizant of the relative lifelong risks and benefits of repeat examinations under anesthesia in young patients.

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#### Curr Psychiatry Rep. 2014;16.

THE COMPLICATED RELATIONSHIP BETWEEN ATTENTION DEFICIT/HYPERACTIVITY DISORDER AND SUBSTANCE USE DISORDERS TOPICAL COLLECTION ON CHILD AND ADOLESCENT DISORDERS. *Zulauf CA, Sprich SE, Safren SA, et al.* 

Adolescents and young adults with substance use disorders (SUD) and attention deficit/hyperactivity disorder (ADHD) are increasingly presenting in clinical practice. The overlap and role of treatment for these co-occurring disorders remains unclear. A review of the literature was conducted to highlight and update recent evidence on the overlap of ADHD and SUD, the

role of ADHD medication on later SUD, and the treatment of ADHD and SUD in adolescents and young adults. Recent work continues to highlight the high risk for comorbid ADHD in patients with SUD; and conversely, the high risk for SUD developing in ADHD across the lifespan, particularly in the context of comorbid conduct disorder. Although the data remains discordant, it appears that ADHD pharmacotherapy does not increase the risk for SUD. Medication treatment alone does not appear to be particularly effective in treating SUD in currently active substance abusing individuals with ADHD. Structured therapies may be effective in treating adolescents and young adults with ADHD and SUD. Further controlled trials evaluating the sequence and effect of structured psychotherapies and/or ADHD pharmacotherapy on SUD relapse in these groups are warranted.

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#### Emot Behav Difficulties. 2014.

DOING BEING BOYS WITH ADHD: CATEGORY MEMBERSHIPS AND DIFFERENCES IN SEN CLASSROOM PRACTICES.

#### Evaldsson AC.

This paper builds on sociological assumptions that teachers, schools and schooling may play an important role in the recognition and psychopathologization of particular boys as 'difficult, disordered and disturbed'. The data draw on ethnographic work combined with video recordings of everyday classroom practices in a special educational needs unit with boys diagnosed with ADHD (Attention Deficit Hyperactivity Disorder). Drawing on ethnomethodological work on members' understanding of social categories (MCA) combined with the related methodology of 'doing difference', the focus is on the local social process through which boys' unruly behaviors are made sense of and treated as the grounds for shifting categorization practices. It is found that both teachers and boys orient to the institutional categories Teacher and Student in teacher-student interactions for the ordering of the classroom. The boys' conduct is in these instances far from pathological but is meaningful in the sense that it provides local resources to resist teacher authorithy and display agency. Overall, the analysis highlights the complexity of locally accomplished identity practices - in terms of how institutional-, gender- and age-appropriate conduct meshes with diagnostic criteria - in the social identification of boys diagnosed with ADHD.

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#### Emot Behav Difficulties. 2014.

DEFINING STUDENT DIVERSITY: CATEGORIZING AND PROCESSES OF MARGINALIZATION IN SWEDISH SCHOOLS.

#### Hjorne E, Saljo R.

The article presents an analysis of how diversity is defined and attended to in Swedish schools. The research reported has been carried out as a case study of categorizing practices that concern the uses of neuropsychiatric diagnoses, notably ADHD. The data were collected as part of a larger study. The interaction over a two-year period between the parents of a boy (William, aged 5.5 years) and representatives of the school (school psychologist, principal, teacher etc.) has been analysed. It is shown that parents and professionals provide different accounts of William's difficulties. The parents, while not denying that their son causes problems in class, argue that the boy will mature and that the problems will disappear. The representatives of the school try to convince the parents that a neuropsychiatric examination of the boy will be beneficial to all parties. The long process of negotiation can be understood as a rhetorical drama, where the

category 'ADHD' serves as the resolution of a complex institutional problem in the modern welfare state.

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#### European Child & Adolescent Psychiatry. 2014.

**ADHD** AND OVERWEIGHT IN BOYS: CROSS-SECTIONAL STUDY WITH BIRTH WEIGHT AS A CONTROLLED FACTOR.

#### Hanc T, Slopien A, Wolanczyk T, et al.

Population studies indicate a strong relationship between birth weight (BW) and body size in later life. However, BW as a variable was never accounted for in studies on the relationship between attention-deficit/hyperactivity disorder (ADHD) and overweight. This study aims to assess the relationship between ADHD and overweight with control of birth weight and other confounding factors. Prevalence of overweight was compared in clinical sample of 219 boys with ADHD and 396 boys without ADHD, aged 6-18 years. The following factors were controlled: BW, parents income and education level, place of residence, ADHD type, selected comorbid disorders and stimulant treatment. Overweight and obesity were diagnosed according to the criteria proposed by the International Obesity Task Force. Logistic regression analysis was used to estimate the association between ADHD and the prevalence of overweight and obesity. Boys with ADHD differed significantly from the control group in distribution of low BW (8.2 vs. 3.0 %, (chi)2=8.23, p=0.02). Low BW was associated with a lower prevalence of overweight than normal and high BW (0 vs. 12.14 %, (chi)2=4.12, p=0.04). Overweight was observed significantly more often in boys with ADHD (17.3 vs. 8.3 %, (chi)2 = 11.23, p<0.001) even after adjustment for BW and other variables (OR=2.44, 95 % CI 1.38-4.29, p=0.002) and after controlling for ADHD type, stimulant treatment and selected comorbid disorders. Independently to applied analysis, obesity was not associated with ADHD. Lower birth weight is over twice more often observed in boys with ADHD than in control group. Although this phenomenon may reduce the rate of overweight in the studied group, ADHD remains strongly associated with increased prevalence of overweight.

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#### European Child & Adolescent Psychiatry. 2014.

# EMPATHY AND PROSOCIAL BEHAVIOR IN RESPONSE TO SADNESS AND DISTRESS IN 6- TO 7-YEAR OLDS DIAGNOSED WITH DISRUPTIVE BEHAVIOR DISORDER AND ATTENTION-DEFICIT HYPERACTIVITY DISORDER.

#### Deschamps PKH, Schutter DJLG, Kenemans JL, et al.

Empathy has been associated with decreased antisocial and increased prosocial behavior. This study examined empathy and prosocial behavior in response to sadness and distress in disruptive behavior disorder (DBD) and attention-deficit hyperactivity disorder (ADHD). Six- and 7-year-old children with DBD (with and without ADHD) (n=67) and with ADHD only (n=27) were compared to typically developing children (TD) (n=37). Parents and teachers rated affective empathy in response to sadness and distress on the Griffith Empathy Measure. Children reported affective empathic ability in response to sad story vignettes. Empathy-induced prosocial behavior in response to sadness and distress was assessed with a computer task, the Interpersonal Response Task (IRT). Compared to TD, children with DBD (with and without ADHD) and those with ADHD only were rated as less empathic by their teachers, but not by their parents. No differences between groups were observed in children who reported affect correspondence. Children with DBD (with and without ADHD) showed less prosocial behavior in response to sadness and distress with ADHD only did not differ from TD. An

additional analysis comparing all children with a diagnosis to the TD group revealed that the difference in prosocial behavior remained after controlling for ADHD symptoms, but not after controlling for DBD symptoms. These findings of impaired empathy-induced prosocial behavior in response to sadness and distress in young children with DBD suggest that interventions to ameliorate peer relationships may benefit from targeting on increasing prosocial behavior in these children.

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#### European Child & Adolescent Psychiatry. 2014.

## BEHAVIORAL SLEEP PROBLEMS AND INTERNALIZING AND EXTERNALIZING COMORBIDITIES IN CHILDREN WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.

#### Lycett K, Sciberras E, Mensah FK, et al.

Behavioral sleep problems are common in children with attention-deficit/hyperactivity disorder (ADHD), as are internalizing and externalizing comorbidities. The prevalence of these difficulties and the extent to which they co-exist in children with ADHD could inform clinical practice, but remains unclear. Therefore, we examined the association between sleep problems and internalizing and externalizing comorbidities in children with ADHD. Children aged 5-13 years were recruited from 21 pediatric practices across Victoria, Australia (N=392). Internalizing and externalizing comorbidities (none, internalizing, externalizing, co-occurring) were assessed by the telephone-administered Anxiety Disorders Interview Schedule for Children IV/Parent version. Sleep problem severity was assessed by primary caregiver report (no, mild, moderate or severe problem). Moderate/severe sleep problems were confirmed using International Classification of Sleep Disorders. Seven specific sleep problem domains (bedtime resistance, sleep anxiety, sleep onset delay, sleep duration, night waking, parasomnias and daytime sleepiness) were assessed using the Children's Sleep Habits Questionnaire. Data were analyzed using adjusted logistic and linear regression models. Compared to children without comorbidities, children with co-occurring internalizing and externalizing comorbidities were more likely to have moderate/severe sleep problems (adjusted OR 2.4, 95 % CI 1.2; 4.5, p=0.009) and problematic sleep across six of seven sleep domains. Children with either comorbidity alone were not at risk of moderate/severe sleep problems, but at the sleep domain level, children with internalizing alone had more sleep anxiety, and those with externalizing alone had less night waking. In conclusion, children with ADHD experiencing co-occurring internalizing and externalizing comorbidities are at an increased risk of sleep problems.

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#### European Child & Adolescent Psychiatry. 2014.

SERUM MATRIX METALLOPROTEINASE-9 LEVELS AND SEVERITY OF SYMPTOMS IN BOYS WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER ADHD/HYPERKINETIC DISORDER HKD. Kadziela-Olech H, Cichocki P, Chwiesko J, et al.

The serum levels of matrix metalloproteinase-9 (MMP-9) in neuropsychiatric disorders of adults have been widely investigated. So far, no studies have been conducted on the relationship of MMP-9 and cognitive domains in children with two phenotype models, attention deficit/hyperactivity disorder and hyperkinetic disorder (ADHD/HKD). The aim of this research was to evaluate and test the hypothesis that serum MMP-9 levels are associated with the severity of symptoms in children with ADHD/HKD and to compare the results in two models of this disorder. The study group comprised 37 Caucasian boys aged 7-12 years with HKD, being a subset of the combined ADHD subtype. Intellectual functions were measured using Wechsler

Intelligence Scale for Children-Revised. The analysis of serum concentrations of MMP-9 was based on a quantitative sandwich ELISA. The statistical regression analysis revealed a correlation between increased serum MMP-9 levels and severity of symptoms in the ADHD ((beta)=0.33; p=0.043) and HKD ((beta)=0.34, p=0.037) model. According to the results, elevated levels of serum MMP-9 in boys with HKD may be associated with clinical impulsivity domain ((beta)=0.38; p=0.019).

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#### Eur Child Adolesc Psychiatry. 2014;1-10.

COMPARISON OF NEUROPSYCHOLOGICAL PERFORMANCES AND BEHAVIORAL PATTERNS OF CHILDREN WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER AND SEVERE MOOD DYSREGULATION.

#### Uran P, Kilic BG.

We aimed to investigate the similarities and differences in neuropsychological test performance, demographic features and behavioral patterns of children and adolescents with the attention deficit hyperactivity disorder combined type (ADHD-C), and the severe mood dysregulation (SMD). Study includes 112 children: 67 with ADHD-C, 24 with SMD and 21 healthy controls. These groups were identified by using the schedule for affective disorders, and schizophrenia for the school-age children-present and lifetime version (KSADS-PL) and the K-SADS-PL-SMD Module. Conners' Parent and Teacher Rating Scale-revised long form (CPRS-R:L and CTRS-R:L) and neuropsychological tests were administered to the research groups. ADHD-C group's performances in Wisconsin Card Sorting Test, Trail Making Test, Stroop Test TBAG form and Controlled Oral Word Association Test were significantly poorer than the control group's performances (p < 0.05). Performance of the SMD group was only descriptively intermediate between performances of the ADHD-C and control group. In the "Oppositional", "Hyperactivity", "Social Problems", "Impulsive", "Emotional Lability" and "Conners' Global Index" subscales of CPRS-R:L, the average scores of the SMD group were significantly higher than the ADHD-C and control group's average scores (p < 0.05). ADHD-C group (but not SMD) could be significantly differentiated from healthy controls with the neuropsychological tests used. SMD group could be differentiated from the ADHD-C and healthy control groups with CPRS-R:L; i.e., ADHD-C versus SMD could be differentiated at the behavioral level only. (copyright) 2014 Springer-Verlag Berlin Heidelberg

#### Eur Neuropsychopharmacol. 2014;24:S74-S75.

#### FACE AND EMOTION RECOGNITION IN CHILDREN WITH ADHD AND AUTISM SPECTRUM DISORDERS: **EFFECTS OF METHYLPHENIDATE.**

#### Placini F, Peddis C, Carucci S, et al.

Objective: The object of this study was to compare Autism Spectrum Disorders (ASD), Attention Deficit Hyperactivity Disorder (ADHD) and Typically Developing Children (TDC) while processing facial emotions and matching emotions by using the Amsterdam Neuropsychological Test battery (ANT). We also examined the influence of treatment with methylphenidate in ADHD patients performing the same ANT tasks. Patterns and timing of recognition of emotional facial expression are potential markers of cognitive dysfunction in both ADHD and ASD: reaction time (RT) studies provide ample evidence that processing speed is a sensitive parameter in the experimental and clinical evaluation of neuropsychological functions [1,2]. Few studies, however, have been designed to compare these patterns in both ASD and ADHD children using the same neuropsychological tasks.

**Methods**: Facial Recognition (FR), Identification Facial Emotion (IFE) and Matching Facial Emotion (MFE) were assessed in 35 drug-free ADHD, 31 ASD and 36 TDC aged 6 to 14 and IQ>70 by reaction time (RT) correct (RTC), RT to errors (RTE) and Errors. FR consists of processing neutral faces; IFE includes eight emotions: happy, sad, angry, fear (four basic emotions), disgust, surprise, shame, and contempt (four complex emotions); MFE task includes four basic emotions. Data about performance in the same tasks for a subgroup of ADHD patients before and during MPH treatment have also been collected. Statistical analyses were performed using SPSS. A multifactorial analysis of variance (MANOVA) was used for comparisons between sets of data in order to examine group differences. Pearson correlations were carried out between the different emotion variables and the IQ, age, C-GAS and CGI.

**Results**: We examined the effect of the three contrasting tasks with respect to Emotional processing using three dependent variables: Reaction Time of correct answers (RTc), RT of errors (RTe) and errors. ADHD children were significantly slower and less accurate than TDCs in both FR and IFE tasks. A significant main effect for group, task and a significant interaction between task and group were found for the FR versus IFE task for both RT and number of errors. Both the ASD and ADHD groups compared with the TDC group were slower; difference in RT between IFE and FR tasks was significant in the ADHD compared with TDC group. Findings could not be explained by a speed-accuracy trade-off difference between groups or by IQ. Analyses about the effect of methylphenidate in a subgroup of ADHD patients are in due course and will be presented during the poster session.

**Conclusions**: The results suggest that specific information processing deficits are present in both ADHD and ASD participants compared to TDC (slower reaction time and larger error rates) especially during face recognition and identification of facial emotions stimuli, having specific differences in processing facial emotions. Methylphenidate possibly exerts a significant effect on the performance of ADHD children. In clinical population such as for ADHD and ASD children, specific neuropsychological tasks should be administered to better characterize specific strengths and difficulties in their cognitive functioning and, in turn, to develop efficient treatment strategies for improving social abilities.

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Eur Neuropsychopharmacol. 2014;24:S84-S85.

# **S**TRUCTURAL BRAIN CORRELATES OF ATYPICAL ANTIPSYCHOTIC AUGMENTATION TO METHYLPHENIDATE TREATMENT IN ADOLESCENTS WITH **ADHD**.

#### Schweren L, Hartman C, Hoekstra P, et al.

Attention-deficit/hyperactivity disorder (ADHD) is a common neurodevelopmental disorder, characterized by age-inappropriate and impairing levels of hyperactivity- impulsivity and/or inattentiveness. Methylphenidate is the first-choice pharmacological treatment for ADHD symptoms. Methylphenidate treatment has been shown to have long-term normalizing effects on fronto-striatal changes in brain structure associated with ADHD [1]. A subgroup of ADHD patients receives atypical antipsychotics concurrent with methylphenidate treatment. The synaptic effects of the two substances are opposing: methylphenidate increases dopamine levels in the synapse, while atypical antipsychotics block the effects of dopamine postsynaptically [2]. The structural brain correlates of long-term combined treatment with methylphenidate and atypical antipsychotics in ADHD patients have not yet been investigated. As part of a large observational multicenter study (NeuroIMAGE), structural MRI images were obtained from ninety-three subjects in three age- and gendermatched samples (84% male, mean age 16.7 years): 31 ADHD patients who had received combined methylphenidate and atypical antipsychotic treatment for a minimum duration of 30 days; 31 patients who had received methylphenidate monotherapy for a minimum

duration of 30 days, and 31 healthy control subjects with no history of psychoactive medication. The majority of patients in the combined treatment group had been treated with risperidone (n=23); other antipsychotics were pipamperone (n=7), quetiapine (n=1), olanzapine (n=1), and aripiprazole (n=1). Treatment duration (either methylphenidate treatment or combined treatment) ranged from 0.1 to 12.1 years, and age of treatment initiation ranged from 2.6 to 17.2 years old. FreeSurfer software was used to calculate total cortical and subcortical volume, as well as volumes of seven frontal cortical and eight subcortical regions of interest, each involved in dopaminergic neurotransmission. Multilevel Linear Mixed Models were applied to analyze between-group differences. Patients in the combined treatment group, but not those in the methylphenidate monotherapy group, showed reduction in total cortical volume compared to healthy control subjects. Total cortical volume reduction was reflected in volume decreases in the bilateral precentral gyrus, the orbitofrontal gyrus, and the inferior, middle and superior frontal gyrus. Subcortically, the combined treatment group but not the methylphenidate monotherapy group showed volume reduction in the bilateral ventral diencephalon and the left thalamus. No striatal changes were found in either of the ADHD groups. The combined treatment group displayed more ADHD symptoms than the methylphenidate monotherapy group, but ADHD severity did not account for the differences in brain structure between the two treatment groups. Concluding, combined methylphenidate and atypical antipsychotic treatment is associated with structural brain changes in the dopaminergic system. These changes are absent or attenuated in patients treated with methylphenidate monotherapy, and cannot be accounted for by the higher number of ADHD symptom in the combined treatment group. Possibly, concurrent antipsychotic treatment may counteract the normalizing effect of methylphenidate on the frontal cortex in ADHD patients. The current investigation is limited by its observational nature.

#### Health Econ. 2014;23:159-81.

### THE EFFECTS OF CHILDHOOD ADHD ON ADULT LABOR MARKET OUTCOMES.

#### Fletcher JM.

Although several types of mental illness, including substance abuse disorders, have been linked with poor labor market outcomes, no current research has been able to examine the effects of childhood attention deficit/hyperactivity disorder (ADHD). Because ADHD has become one of the most prevalent childhood mental conditions, it is useful to understand the full set of consequences of the illness. This article uses a longitudinal national sample, including sibling pairs, to show the important labor market outcome consequences of ADHD. The employment reduction is between 10 and 14 percentage points, the earnings reduction is approximately 33%, and the increase in social assistance is 15 points, figures that are larger than many estimates of the Black people/White people earnings gap and the gender earnings gap. A small share of the link is explained by educational attainments and co-morbid health conditions and behaviors. The results also show important differences in labor market consequences by family background and age of onset. These findings, along with similar research showing that ADHD is linked with poor education outcomes and adult crime, suggest the importance of treating childhood ADHD to foster human capital.

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#### Hum Brain Mapp. 2014. NETWORK CONNECTIVITY ABNORMALITY PROFILE SUPPORTS A CATEGORICAL-DIMENSIONAL HYBRID MODEL OF ADHD.

#### Elton A, Alcauter S, Gao W.

Attention-deficit/hyperactivity disorder (ADHD) is characterized by inattention, hyperactivity, and impulsivity, but there is no consensus regarding whether ADHD exists on the extreme end of a continuum of normal behavior or represents a discrete disorder. In this study, we sought to characterize both the categorical and dimensional variations in network functional connectivity in order to identify neural connectivity mechanisms of ADHD. Functional connectivity analyses of resting-state fMRI data from 155 children with ADHD and 145 typically developing children (TDC) defined the dorsal attention network (DA), default mode network (DM), salience processing network (SAL) and executive control network (CON). Regional alterations in connectivity associated with categorical diagnoses and dimensional symptom measures (inattention and hyperactivity/impulsivity) as well as their interaction were systematically characterized. Dimensional relationships between symptom severity measures and functional connectivity that did not differ between TDC and children with ADHD were observed for each network, supporting a dimensional characterization of ADHD. However, categorical differences in functional connectivity magnitude between TDC and children with ADHD were detected after accounting for dimensional relationships, indicating the existence of categorical mechanisms independent of dimensional effects. Additionally, differential dimensional relationships for TDC versus ADHD children demonstrated categorical differences in brain-behavior relationships. The patterns of network functional organization associated with categorical versus dimensional measures of ADHD accentuate the complexity of this disorder and support a dual characterization of ADHD etiology featuring both dimensional and categorical mechanisms.

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#### Indian Pediatr. 2014;51:151-52.

#### ATTENTION DEFICIT HYPERACTIVITY DISORDER IN ADOLESCENT SCHOOL CHILDREN. Juneja M, Sairam S, Jain R.

The prevalence of Attention deficit hyperactivity disorder was estimated in 500 adolescents using Conners parents and teachers rating scales. Thirty six (7.2%) adolescents had positive scores on both the scales. The parents and teachers also completed a Diagnostic and Statistical Manual-IV based questionnaire which showed good agreement with Conners rating scales.

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#### Innov Clin Neurosci. 2013;10:19-22.

INSOMNIA AND ATTENTION DEFICIT HYPERACTIVITY DISORDER IN PEDIATRICS: A CHECKLIST FOR PARENTS.

#### Yarlagadda A, Connell MA, Kasaraneni J, et al.

Attention deficit hyperactivity disorder is a commonly diagnosed condition in the pediatric as well as adult psychiatric population. Attention deficit hyperactivity disorder has undoubtedly been over diagnosed and treated with both stimulants and non-stimulants over the past few decades. Behavior problems in children are commonly noticed both by parents and teachers, leading to the formulation of attention deficit hyperactivity disorder diagnosis. Insomnia, on the other hand, is not as readily detected by parents and may result in behavioral problems at school. Several medical conditions responsible for causing insomnia may need to be ruled out before the diagnosis of attention deficit hyperactivity disorder is confirmed. In this article, we highlight

symptoms common both to insomnia and attention deficit hyperactivity disorder by development of a checklist to help delineate the two conditions. The purpose of this checklist is to provide informational and educational tools both for parents and teachers to distinguish insomnia from attention deficit hyperactivity disorder. The ultimate goal of this paper is to improve diagnostic screening for attention deficit hyperactivity disorder by excluding conditions such as insomnia that may masquerade as attention deficit hyperactivity disorder.

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#### Int J Epidemiol. 2014;43:83-90.

# MATERNAL PRE-PREGNANCY BODY MASS INDEX AND OFFSPRING ATTENTION DEFICIT HYPERACTIVITY DISORDER: A POPULATION-BASED COHORT STUDY USING A SIBLING-COMPARISON DESIGN. *Chen Q, Sjolander A, Langstrom N, et al.*

# **Background**: High maternal pre-pregnancy body mass index (BMI) is associated with increased risk of offspring attention deficit hyperactivity disorder (ADHD). However, the role of unmeasured familial confounding for this association remains unclear.

**Methods**: We conducted a population-based cohort study via linkage of Swedish national and regional registers to investigate maternal pre-pregnancy BMI (underweight: BMI <18.5; overweight: 25 (less-than or equal to) BMI <30; obesity: BMI (greater-than or equal to)30) in relation to offspring ADHD. We followed 673 632 individuals born in Sweden between 1992 and 2000, with prospectively collected information on maternal prepregnancy BMI, until they received an ADHD diagnosis or ADHD medication, death, emigration or 31 December 2009. Hazard ratios (HRs) were estimated by Cox proportional hazards models. Stratified Cox proportional hazards models were applied to data on full siblings to control for unmeasured familial confounding.

**Results**: At the population level, pre-pregnancy overweight/obesity was associated with increased risk of offspring ADHD (HRoverweight=1.23, 95% Cl=1.18-1.27, P=0.01; HRobesity=1.64, 95% Cl=1.57-1.73, P=0.01), after adjustment for measured covariates. In full sibling comparisons, however, previously observed associations no longer remained (HRoverweight=0.98, 95% Cl=0.83-1.16, P=0.82; HRobesity=1.15, 95% Cl=0.85-1.56, P=0.38). **Conclusions**: The results suggested that the association between maternal prepregnancy overweight/obesity and offspring ADHD could be ascribed to unmeasured familial confounding.

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#### Iran J Psychiatry. 2014;9:25-30.

# A COMPARISON OF EFFECTIVENESS OF REGULATION OF WORKING MEMORY FUNCTION AND METHYLPHENIDATE ON REMEDIATION OF ATTENTION DEFICIT HYPERACTIVITY DISORDER (ADHD). *Mohammadi MR*, Soleimani AA, Farahmand Z, et al.

Attention Deficit/Hyperactivity Disorder (ADHD) is a prevalent and serious disorder affecting such key cognitive components as working memory. Working memory serves to facilitate and check attention in any individual and to focus on those affairs that need to be retained in mind. This study examines whether a combination of the two therapeutic methods of working memory training and Methylphenidate might be more effective in treating ADHD in children aged 6 to 12 years of age than when methylphenidate is applied alone. Method: Subjects of the study are 48 children suffering from ADHD. They were selected by random sampling. The experimental group included 23 children with ADHD who received a combination of working memory training and Methylphenidate, and the control group which included 25 children with ADHD received Methylphenidate only. To check the effects of the intervention, Conners' Parent Rating Scale (CPRS-48) was applied before and after the intervention. After intervention, data were collected

from the remaining samples in the two groups. Data were examined both through descriptive statistical methods and analytic statistical methods, including T-student test and Quantile-Quantile Plots diagram. Results: The study demonstrated that a combination of the cognitive intervention of working memory training and methylphenidate is more effective in alleviating ADHD symptoms rather than when methylphenidate is applied in isolation. In the CPRS pre-test and post-test, the mean difference of the experimental and the control group was 8.39 and 1.88 respectively, indicating that the working memory group has improved more than the control group. Conclusions: The study reveals that the ADHD symptoms were more contained in the test group than the control group due to working memory training. The cognitive intervention through working memory training may be effective in alleviating the severity of disorder measured in the pre-test.

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#### J AAPOS. 2014;18:10-14.

# PREVALENCE OF ATTENTION-DEFICIT/HYPERACTIVITY DISORDER AMONG CHILDREN WITH VISION IMPAIRMENT.

#### Decarlo DK, Bowman E, Monroe C, et al.

**Purpose** To evaluate the prevalence of parent-reported attention-deficit/ hyperactivity disorder (ADHD) in two clinics in Alabama serving children with vision impairment.

**Methods** The medical records of children 4-17 years of age attending the Alabama School for the Blind (ASB) during the 2010-2011 school year or seen at the University of Alabama at Birmingham (UAB) Center for Low Vision Rehabilitation between 2006 and 2010 were retrospectively reviewed. Sociodemographics, ocular characteristics, and parental report of ADHD diagnosis were obtained. The prevalence of ADHD was compared to national and state figures for age-similar children regardless of comorbidities. The prevalence of ADHD, sociodemographic, and ocular characteristics was also compared between clinical sites.

**Results** A total of 264 children participated in the study (95 from ASB and 169 from UAB). The prevalence of ADHD among children with visual acuity better than hand motion (n = 245) was 22.9%, which is higher than reported state (14.3%) and national prevalence (9.5%) for children in this age range. The prevalence was similar at ASB (22.4%) and UAB (23.1%). Those with ADHD were similar to those without ADHD with respect to age, sex, and race. Children with ADHD were significantly less likely to have nystagmus and more likely to have better visual acuity (P < 0.05). The prevalence of ADHD among the 19 participants with total or near total vision loss (all from ASB) was 10.5%.

**Conclusions** Our analyses suggest that children with vision impairment may be more likely to be diagnosed with ADHD than children in the general population.

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Journal of Attention Disorders. 2014 Jan;18:52-60.

THE IMPACT OF PERSISTING HYPERACTIVITY ON SOCIAL RELATIONSHIPS: A COMMUNITY-BASED, CONTROLLED 20-YEAR FOLLOW-UP STUDY.

#### Moyá J, Stringaris AK, Asherson P, et al.

**Objective**: The purpose of this study was to examine whether persisting hyperactivity into adulthood was associated with impaired family, friendship, and partner relationships or poor coping skills in everyday life.

**Method**: A 20-year community-based follow-up of 6- to 7-year-old boys showing pervasive hyperactivity (n=40) and unaffected controls (n=25) was conducted. At age 27 years, participants were assessed with detailed interview techniques as well as self-report ratings.

**Results**: ADHD in adulthood was associated with problems in intimate relationships and negotiation skills. Antisocial behavior did not influence the association, but remitting childhood hyperactivity was not associated with social relationship difficulties in adulthood.

**Conclusion**: In an untreated, community-based sample of hyperactive children, the risk for unsatisfactory social relationships is largely confined to those patients who still show ADHD in adulthood. The majority of patients who experience childhood hyperactivity have positive social relationships in adulthood.

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#### Journal of Attention Disorders. 2014 Jan;18:23-30.

LONG-TERM TEMPORAL STABILITY OF MEASURED INATTENTION AND IMPULSIVITY IN TYPICAL AND REFERRED CHILDREN.

#### Mayes SD, Gordon M, Calhoun SL, et al.

**Objective**: This study investigates the stability of measured inattention and impulsivity in children. **Method**: The Gordon Diagnostic System (GDS) assesses inattention and impulsivity and has been administered in the same manner since its 1983 publication. GDS scores were compared between the 1983 standardization sample and a recent typical sample of 445 children, 562 children with ADHD-Combined (ADHD-C) type, 235 with ADHD-Inattentive (ADHD-I) type, and 231 with autism.

**Results**: Typical children earned a GDS composite standard score of 100, consistent with the normal mean of 100 in the 1983 standardization sample. Means for children with ADHD-C, ADHD-I, and autism were 70, 78, and 76, respectively, approximately two standard deviations below the normal mean.

**Conclusion**: As measured by the GDS, children are no more or less inattentive and impulsive today than in 1983, suggesting that inattention and impulsivity are stable neurobiological traits largely unaffected by cultural, educational, and environmental factors.

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Journal of Attention Disorders. 2014 Jan;18:61-72.

ASSOCIATION BETWEEN CHILDHOOD SPECIFIC LEARNING DIFFICULTIES AND SCHOOL PERFORMANCE IN ADOLESCENTS WITH AND WITHOUT ADHD SYMPTOMS: A 16-YEAR FOLLOW-UP.

#### Taanila A, Ebeling H, Tiihala M, et al.

**Objective**: The authors investigated whether childhood specific learning difficulties (SLDs) predict later school performance in adolescents with ADHD symptoms (ADHDs) and how SLDs associate with educational aspirations.

**Method**: In the Northern Finland Birth Cohort 1986 (n=9,432), data about children were collected using questionnaires for parents and teachers at ages 7 and 8 and for parents and adolescents at ages 15/16. Information on school performance was obtained from a national register.

**Results**: The occurrence of SLDs at 8 years was 19.9% (n=1,198), ADHDs at 15/16 years was 8.0% (n=530), and comorbid ADHDs and SLDs was 3.0% (n=179). Having ADHDs but not SLDs or having both was associated with a significantly lower mean value in school grades for theoretical subjects. Adolescents with comorbid ADHDs and SLDs repeated a grade more often, and their educational aspirations were less ambitious than those in other groups.

**Conclusion**: ADHDs and SLDs have a negative influence on academic achievements.

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Journal of Attention Disorders. 2014 Jan;18:31-43.

PERCEIVED SOCIAL ACCEPTANCE AND PEER STATUS DIFFERENTIALLY PREDICT ADJUSTMENT IN YOUTH WITH AND WITHOUT **ADHD**.

#### McQuade JD, Vaughn AJ, Hoza B, et al.

**Objective**: This study extends previous research and examined if the longitudinal relation between self-perceived social acceptance and changes in adjustment was moderated by peer status and ADHD diagnosis.

**Method**: A sample of children with ADHD and a normative comparison group (age 8-13 years) were assessed at baseline and one-year follow-up. Self-perceived social acceptance, peer status, and three areas of adjustment (depression symptoms, aggression/conduct problems, and social skills) were measured.

**Results**: Moderation was found when predicting depression symptoms and aggression/ conduct problems. Specifically, in children with ADHD only, higher perceived social acceptance protected against increases in depression symptoms for those with lower peer preference, but predicted greater aggression/conduct problems for those with higher peer preference. There was not evidence of significant moderation for predicting social skills; instead non- ADHD status, greater peer preference, and greater self-perceived social acceptance were each predictive of greater social skills.

**Conclusion**: Results highlight the complex association between positive social self-perceptions and adjustment for children with ADHD and caution against a universal assumption that high self-perceptions are adaptive.

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Journal of Attention Disorders. 2014 Jan;18:14-22.

#### EARLY MARKERS IN INFANTS AND TODDLERS FOR DEVELOPMENT OF ADHD.

#### Gurevitz M, Geva R, Varon M, et al.

**Objective**: Characterization of risk factors for ADHD in infancy may enable early intervention to diminish the symptoms that ensue.

**Method**: In a retrospective study, the well-baby-care clinic records from birth to 18 months of age of 58 children diagnosed at school age for ADHD were compared with those of 58 control children, and the differences between the two groups were statistically analyzed.

**Results**: Eight parameters during infancy were found to be significantly associated with later development of ADHD: at 0 to 1 month—advanced maternal age, lower maternal education, family history of ADHD, and social problems; at 3 and 18 months—decrease in head circumference percentile; at 9 and 18 months—delay in motor and language development, and difficult temperament. The predictive regression model accounted for 58% of the variance.

**Conclusion**: This study highlights early risk markers in infants and toddlers that may predict the development of ADHD.

Journal of Attention Disorders. 2014 Jan;18:3-13.

A NATIONAL EPIDEMIOLOGICAL STUDY OF OFFENDING AND ITS RELATIONSHIP WITH ADHD SYMPTOMS AND ASSOCIATED RISK FACTORS.

#### Gudjonsson GH, Sigurdsson JF, Sigfusdottir ID, et al.

**Objective**: The objective was to disentangle the relationship between offending, ADHD, and comorbid risk factors.

**Method**: A total of 11,388 students in further education completed a questionnaire, which measured nonviolent and violent delinquency, current ADHD symptoms, conduct disorder, substance use, association with delinquent peers, emotional lability, anger problems, violent attitudes, and low self-esteem.

**Results**: The nonviolent and violent delinquency measures correlated significantly with all the predictor measures, with small to large effect sizes. Multiple regressions showed that after controlling for age and gender, ADHD contributed 8.2% and 8.8% to the variance in nonviolent and violent delinquency, respectively, but these effects were largely mediated by the comorbid measures, particularly substance use, association with delinquent peers, and conduct disorder.

**Conclusion**: The relationship between ADHD symptoms and offending among young people is largely explained indirectly by comorbid factors. A key prevention is to address substance use problems and association with delinquent peers.

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Journal of Attention Disorders. 2014 Jan;18:44-51.

NAVIGATING ADOLESCENCE: AN EPIDEMIOLOGICAL FOLLOW-UP OF ADAPTIVE FUNCTIONING IN GIRLS WITH CHILDHOOD ADHD SYMPTOMS AND CONDUCT DISORDER.

#### Deane H, Young S.

**Objective**: The current study investigated the experience of girls growing up with cognitive and social disorders.

**Method**: Eight adolescent girls participated in interviews that were transcribed and analyzed using Interpretative Phenomenological Analysis.

**Results**: Four of the girls had a history of ADHD symptoms and conduct disorder problems (ADHD/CP), four did not. Three master themes emerged within the domain of "Coping Behaviors": seeking social support, bravado, and avoidance. Three master themes emerged within the domain of "Barriers to Adaptive Functioning": lack of support and guidance, poor negotiation of interpersonal conflict, and victimization. Although all participants experienced developmental barriers, the girls with ADHD/CP coped with these barriers in a less effective way.

**Conclusion**: The study raises an important developmental concern, the seemingly ineffective coping strategies of ADHD/CP adolescents.

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Journal of Child Psychology and Psychiatry. 2014 Mar;55:247-55.

# A RANDOMIZED CLINICAL TRIAL OF COGMED WORKING MEMORY TRAINING IN SCHOOL-AGE CHILDREN WITH ADHD: A REPLICATION IN A DIVERSE SAMPLE USING A CONTROL CONDITION. *Chacko A, Bedard AC, Marks DJ, et al.*

**Background**: Cogmed Working Memory Training (CWMT) has received considerable attention as a promising intervention for the treatment of Attention-Deficit/Hyperactivity Disorder (ADHD) in children. At the same time, methodological weaknesses in previous clinical trials call into question reported efficacy of CWMT. In particular, lack of equivalence in key aspects of CWMT (i.e., contingent reinforcement, time-on-task with computer training, parent– child interactions, supportive coaching) between CWMT and placebo versions of CWMT used in previous trials may account for the beneficial outcomes favoring CWMT.

**Methods**: Eighty-five 7- to 11-year old school-age children with ADHD (66 male; 78%) were randomized to either standard CWMT (CWMT Active) or a well-controlled CWMT placebo condition (CWMT Placebo) and evaluated before and 3 weeks after treatment. Dependent measures included parent and teacher ratings of ADHD symptoms; objective measures of attention, activity level, and impulsivity; and psychometric indices of working memory and academic achievement (Clinical trial title: Combined cognitive remediation and behavioral intervention for the treatment of Attention-Deficit/Hyperactivity Disorder; http:// clinicaltrials.gov/ct2/show/NCT01137318).

**Results**: CWMT Active participants demonstrated significantly greater improvements in verbal and nonverbal working memory storage, but evidenced no discernible gains in working memory storage plus processing/manipulation. In addition, no treatment group differences were observed for any other outcome measures.

**Conclusions**: When a more rigorous comparison condition is utilized, CWMT demonstrates effects on certain aspects of working memory in children with ADHD; however, CWMT does not appear to foster treatment generalization to other domains of functioning. As such, CWMT should not be considered a viable treatment for children with ADHD.

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Journal of Child Psychology and Psychiatry. 2014 Mar;55:292-300.

THE PERSISTENCE OF COGNITIVE DEFICITS IN REMITTED AND UNREMITTED ADHD: A CASE FOR THE STATE-INDEPENDENCE OF RESPONSE INHIBITION.

#### McAuley T, Crosbie J, Charach A, et al.

**Background**: Response inhibition, working memory, and response variability are possible endophenotypes of ADHD based on their association with the disorder and evidence of heritability. One of the critical although rarely studied criteria for a valid endophenotype is that it persists despite waxing and waning of the overt manifestations of the disorder, a criterion known as state-independence. This study examined whether these aspects of cognition exhibit stateindependence in ADHD.

**Methods**: One hundred and seventy-nine children diagnosed with ADHD in a rigorous baseline assessment were contacted for follow-up assessment in adolescence. Of this sample, 130 (73%) were reascertained. At follow-up, children previously diagnosed with ADHD were identified as remittent (n=24), persistent (n=64), or in partial remission (n=42) based on symptoms and impairment of the disorder. Response inhibition, working memory, and response variability were assessed both in childhood (baseline) and adolescence (follow-up) and were compared with agematched controls (40 children and 28 adolescents) seen at either time point.

**Results**: Relative to controls, ADHD children showed baseline deficits in response inhibition, working memory, and response variability. Only the group difference in response inhibition remained significant in adolescence. In general, cognitive performance among ADHD participants improved with age and did so regardless of changes in ADHD symptoms and impairment. Within the ADHD group, however, cognitive performance in childhood and in adolescence did not differ amongst those with persistent, remittent, and partially remittent forms of the disorder.

**Conclusions**: Results demonstrate that response inhibition not only distinguishes ADHD children from their unaffected peers but is also state-independent, such that deficits remain present irrespective of changes in the disease phenotype. In other words, inhibitory deficits measured in childhood persist into adolescence even when the ADHD phenotype remits.

These findings provide further evidence that the ability to stop prepotent actions is an endophenotype of ADHD.

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#### J Clin Psychiatry. 2014;75:e108-e113.

## ANXIETY AND DISRUPTIVE BEHAVIOR MEDIATE PATHWAYS FROM ATTENTION-DEFICIT/ HYPERACTIVITY DISORDER TO DEPRESSION.

#### Roy A, Oldehinkel AJ, Verhulst FC, et al.

**Objective**: The progression to depression in children with attention-deficit/hyperactivity disorder (ADHD) is not clearly understood. To clarify this relationship, we tested the following hypotheses in a population-based study: (1) children with ADHD have a higher risk of developing depression than children without ADHD; (2) the pathway from ADHD to depression is mediated (partly) through anxiety and disruptive behavior disorders; and (3) mediation through anxiety is more prevalent in girls, and mediation through disruptive behavior disorders is more prevalent in boys.

**Method**: From October 2008 to September 2010, the Composite International Diagnostic Interview was used to assess ADHD, major depressive episodes, anxiety disorders, and disruptive behavior disorders in 1,584 participants from the TRacking Adolescents' Individual Lives Survey (TRAILS) cohort. Cox regression was used to model the effects of ADHD, anxiety, and disruptive behaviors on depression. Risk of and pathways to depression were studied in both children with ADHD and children with subthreshold ADHD.

**Results**: Comorbid depression was present in 36% of children with a diagnosis of ADHD, 24% of children with subthreshold ADHD, and 14% of children with no ADHD. Anxiety and disruptive behaviors mediated 32% of depression in ADHD. Pathways through anxiety and disruptive behavior disorders were independent of gender. Disruptive behavior disorder was a stronger mediator than anxiety for both genders (all P < .01).

**Conclusions**: These findings may help forewarn of impending depression and therefore allow opportunities for interventions when comorbid anxiety and/or disruptive behavior disorders are present in a child with ADHD.

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J Dev Behav Pediatr. 2014 Jan;35:18-27.

NEUROFEEDBACK AND COGNITIVE ATTENTION TRAINING FOR CHILDREN WITH ATTENTION-DEFICIT HYPERACTIVITY DISORDER IN SCHOOLS.

#### Steiner NJ, Frenette EC, Rene KM, et al.

**Objective**: To evaluate the efficacy of 2 computer attention training systems administered in school for children with attention-deficit hyperactivity disorder (ADHD).

**Method**: Children in second and fourth grade with a diagnosis of ADHD (n=104) were randomly assigned to neurofeedback (NF) (n=34), cognitive training (CT) (n=34), or control (n=36) conditions. A 2-point growth model assessed change from pre-post intervention on parent reports (Conners 3-Parent [Conners 3-P]; Behavior Rating Inventory of Executive Function [BRIEF] rating scale), teacher reports (Swanson, Kotkin, Agler, M-Flynn and Pelham scale [SKAMP]; Conners 3-Teacher [Conners 3-T]), and systematic classroom observations (Behavioral Observation of Students in Schools [BOSS]). Paired t tests and an analysis of covariance assessed change in medication.

**Results**: Children who received NF showed significant improvement compared with those in the control condition on the Conners 3-P Attention, Executive Functioning and Global Index, on all BRIEF summary indices, and on BOSS motor/verbal off-task behavior. Children who received CT

showed no improvement compared to the control condition. Children in the NF condition showed significant improvements compared to those in the CT condition on Conners 3-P Executive Functioning, all BRIEF summary indices, SKAMP Attention, and Conners 3-T Inattention subscales. Stimulant medication dosage in methylphenidate equivalencies significantly increased for children in the CT (8.54 mg) and control (7.05 mg) conditions but not for those in the NF condition (0.29 mg).

**Conclusion**: Neurofeedback made greater improvements in ADHD symptoms compared to both the control and CT conditions. Thus, NF is a promising attention training treatment intervention for children with ADHD.

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#### J Environ Public Health. 2014;2014.

# URINARY POLYCYCLIC AROMATIC HYDROCARBON METABOLITES AND ATTENTION/DEFICIT HYPERACTIVITY DISORDER, LEARNING DISABILITY, AND SPECIAL EDUCATION IN U.S. CHILDREN AGED 6 TO 15.

#### Abid Z, Roy A, Herbstman JB, et al.

Exposure to polycyclic aromatic hydrocarbons (PAHs) adversely affects child neurodevelopment, but little is known about the relationship between PAHs and clinically significant developmental disorders. We examined the relationship between childhood measures of PAH exposure and prevalence of attention deficit/hyperactivity disorder (ADHD), learning disability (LD), and special education (SE) in a nationally representative sample of 1,257 U.S. children 6-15 years of age. Data were obtained from the National Health and Nutrition Examination Survey (NHANES) 2001-2004. PAH exposure was measured by urinary metabolite concentrations. Outcomes were defined by parental report of (1) ever doctor-diagnosed ADHD, (2) ever doctor- or school representative-identified LD, and (3) receipt of SE or early intervention services. Multivariate logistic regression accounting for survey sampling was used to determine the associations between PAH metabolites and ADHD, LD, and SE. Children exposed to higher levels of fluorine metabolites had a 2-fold increased odds (95% C.I. 1.1, 3.8) of SE, and this association was more apparent in males (OR 2.3; 95% C.I. 1.2, 4.1) than in females (OR 1.8; 95% C.I. 0.6, 5.4). No other consistent pattern of developmental disorders was associated with urinary PAH metabolites. However, concurrent exposure to PAH fluorine metabolites may increase use of special education services among U.S. children.

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J Fluency Disord. 2014.

STUTTERING IN RELATION TO ANXIETY, TEMPERAMENT, AND PERSONALITY: REVIEW AND ANALYSIS WITH FOCUS ON CAUSALITY.

#### Alm PA.

Anxiety and emotional reactions have a central role in many theories of stuttering, for example that persons who stutter would tend to have an emotionally sensitive temperament. The possible relation between stuttering and certain traits of temperament or personality were reviewed and analyzed, with focus on temporal relations (i.e., what comes first). It was consistently found that preschool children who stutter (as a group) do not show any tendencies toward elevated temperamental traits of shyness or social anxiety compared with children who do not stutter. Significant group differences were, however, repeatedly reported for traits associated with inattention and hyperactivity/impulsivity, which is likely to reflect a subgroup of children who stuttering is

increased by an emotionally reactive temperament in children who stutter. Speech-related social anxiety develops in many cases of stuttering, before adulthood. Reduction of social anxiety in adults who stutter does not in itself appear to result in significant improvement of speech fluency. Studies have not revealed any relation between the severity of the motor symptoms of stuttering and temperamental traits. It is proposed that situational variability of stuttering, related to social complexity, is an effect of interference from social cognition and not directly from the emotions of social anxiety. In summary, the studies in this review provide strong evidence that persons who stutter are not characterized by constitutional traits of anxiety or similar constructs.

**Educational Objectives**: This paper provides a review and analysis of studies of anxiety, temperament, and personality, organized with the objective to clarify cause and effect relations. Readers will be able to (a) understand the importance of effect size and distribution of data for interpretation of group differences; (b) understand the role of temporal relations for interpretation of cause and effect; (c) discuss the results of studies of anxiety, temperament and personality in relation to stuttering; and (d) discuss situational variations of stuttering and the possible role of social cognition.

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#### J Mol Neurosci. 2012;48:S113.

# MULTI-WAY MODELING OF ELECTROENCEPHALOGRAPHIC DATA TO EVALUATE THE TREATMENT EFFECT OF (CONCERTA(REGISTERED TRADEMARK)) ON ADULT PATIENTS WITH ADHD.

#### Spanier AB, Gal N, Shani-Hershkovitch R, et al.

**Background**: ADHD is one of the most common childhood disorders. In the past it was believed that the symptoms subside after adolescence. However, 65% of the children diagnosed with ADHD will in fact grow up to be adults diagnosed with ADHD. While medical treatment may improve many of the main symptoms like distractibility, hyperactivity and impulsiveness, up to 30% of the patients do not respond. Thus research is still required to explore the effect of medical treatment, and the reasons for the response variability, with an emphasis on adults above high school age.

**Methods**: In the present study 12 adults diagnosed with ADHD came to three meetings that took place at the Harvard medical school. EEG was measured during the Go/ NoGo task. In the first meeting the patients performed tasks without taking medicine at all. In the second meeting (week later) they took a single dose of 36 mg and in the third meeting (six weeks later) they each received an individual dosage that was determined by the treating physician. The aim of this research was to compare the EEG profile of the patients with the profile a healthy person as well as the profile of patients under different doses of Methylphenidate (Concerta(registered trademark)). We compared various N-ways models as feature extraction methods in the time domain.

**Results**: The main component of the EEG that distinguished between healthy and ADHD subjects was at the time range of the P3 component. The feature that best distinguished the different visits (characterized by different doses) was at the range of the visual P2-N2 component. **Conclusions**: This study demonstrates that (1) EEG signals of adults with ADHD can be classified by feature extracted from the N-ways models (2) The N-ways models such as TUCKER3 and S-PARAFAC are more efficient as feature extraction methods for those EEG signals as compared to the traditional PARAFAC N-way model.

#### J Nerv Ment Dis. 2014;202:247-52.

# RISK TAKING IN ADOLESCENTS WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER ON A PROBABILISTIC CHOICE TASK.

#### Kroyzer N, Gross-Tsur V, Pollak Y.

Risk taking is commonly attributed to individuals with attention deficit hyperactivity disorder (ADHD). This study investigated whether adolescents with ADHD would choose to take greater risks on a probabilistic task in which contingencies are explicitly presented. Adolescents with and without ADHD, aged 13 to 18 years, performed a modified version of the Cambridge Gambling Task. The subjects with ADHD risked smaller sums and chose the unfavorable outcomes more frequently than did the controls but had the same speed of decision and risk adjustment. The results indicate that their poor decisions were not due to impulsivity or insensitivity to the concept of probability and that increased risk taking is not always associated with ADHD. Moreover, in situations that do not demand learning of contingencies, ADHD may be associated with decreased, rather than increased, risk taking.

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#### J Nerv Ment Dis. 2014.

# PREVALENCE AND CORRELATES OF ATTENTION DEFICIT HYPERACTIVITY DISORDER IN ADULTS FROM A FRENCH COMMUNITY SAMPLE.

#### Caci HM, Morin AJS, Tran A.

Validated tools are lacking in languages such as French to diagnose attention deficit hyperactivity disorder (ADHD) in adults. The Adult ADHD Symptoms Self-Report (ASRS) was filled out by 1171 parents of 900 school-aged youths in the context of the Children and Parents With ADHD and Related Disorders study. Prevalence estimates based on three scoring methods are compared (6-item screener, all 18 items, or the screener followed by the 12 remaining items). On the basis of the recommended and more conservative scoring method, the overall prevalence of ADHD symptoms is estimated to be 2.99%, without significant group differences between sexes or between younger and older adults. Potential correlates of ADHD symptoms were also examined in their relatives (children, brothers/sisters, uncles/aunts, and parents) as follows: birth order, level of education, body mass index categories, enuresis, suicide attempts, depression, and learning disabilities. Adults can be screened for ADHD symptoms using the ASRS; negative long-term outcomes should be assessed in patients' relatives too.

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J Pediatr. 2014;164:675. ADOLESCENTS WITH ADHD DEMONSTRATE DRIVING INCONSISTENCY. Winston FK, McDonald CC, McGehee DV.

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#### J Psychopharmacol. 2014;28:220-26.

NEUROTROPHIN 3 GENOTYPE AND EMOTIONAL ADVERSE EFFECTS OF OSMOTIC-RELEASE ORAL SYSTEM METHYLPHENIDATE (OROS-MPH) IN CHILDREN WITH ATTENTION-DEFICIT/ HYPERACTIVITY DISORDER.

Park S, Kim BN, Kim JW, et al.

Neurotrophin 3 (NTF3) has been studied in relation to the pathophysiology of attentiondeficit/hyperactivity disorder (ADHD) and mood disorders as well as psychostimulant action. We hypothesized that the risk of an emotional side effect to methylphenidate (MPH) treatment may be associated with NTF3 genotypes. Ninety-six medication-naive children with ADHD (mean age 8.70, standard deviation 1.41 years, 79 males) were genotyped and treated with MPH. At baseline, which was prior to MPH treatment, and after two weeks of medication, investigators asked children and their parents or caregivers about adverse events using a symptom rating scale. ADHD subjects with the A/A genotype at the NTF3 rs6332 polymorphism showed the highest 'Emotionality' and 'Over-focus/euphoria' factor scores, followed by those with the G/A genotype and those with the G/G genotype (p=0.042 and p=0.045, respectively). ADHD subjects with the A/A genotype at the NTF3 rs6332 polymorphism showed the highest 'Proneness to crying' and 'Nail biting' item scores, followed by those with the G/A genotype and those with the G/G genotype (p=0.047 and p=0.017, respectively). These data provide preliminary evidence that genetic variation in the NTF3 gene is related to susceptibility to emotional side effects in response to MPH treatment in Korean children with ADHD.

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#### J Psychopharmacol. 2014;28:282-83.

LAMOTRIGINE FOR ATTENTION DEFICIT-HYPERACTIVITY DISORDER COMORBID WITH MOOD DISORDERS: A CASE SERIES.

#### Oncu B, Er O, Colak B, et al.

Attention dei(logical not) cit-hyperactivity disorder (ADHD) is frequently comorbid with mood disorders in both children and adults. Comorbidity is shown to have negative consequences and it needs to be treated effectively. Lamotrigine, an anticonvulsant indicated for the maintenance treatment of bipolar depression is reported to be effective in adult ADHD comorbid with bipolar II disorder. We conducted a retrospective chart review to identify patients with adult ADHD and comorbid mood disorders on lamotrigine, along with ADHD medications, and/or antidepressants and antipsychotics. We identified 40 patients (17 women, 42.5%; age range 16-55 yrs), 50% with bipolar II and 50% with recurrent depression. Their treatment response was evaluated by Clinical Global Impression scales. We found that 31 patients (77.5%) improved with lamotrigine, there was no change in 7 patients (17.5%) and 2 patients got worse, with a mean lamotrigine dose of 125.6 (plus or minus) 47.8 mg (25-250 mg). To our knowledge, this is the first study to report that lamotrigine might be a safe and effective treatment option for adult ADHD comorbid with bipolar and recurrent depression.

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#### J Sleep Res. 2014;23:189-95.

APNEA-RELATED SLEEP FRAGMENTATION AND POOR VIGILANCE IN CHILDREN WITH WELL-CONTROLLED ASTHMA.

#### Yoon HK, Kang SG, Lee HJ, et al.

**Summary**: It has been reported that sleep problems and neurocognitive deficit in asthmatic children is prevalent. However, systematic studies on these problems in stable asthma using polysomnography have rarely been performed. We therefore investigated sleep and neurocognitive functioning in children with well-controlled asthma. Forty-three children with well-controlled, stable asthma and 31 controls (age range: 6-9 years) were enrolled in the study. Subjects were questioned for daytime sleepiness using the Paediatric Daytime Sleepiness Scale. Complete overnight polysomnography and neurocognitive function in comparison to their agematched controls. Asthmatic children had a higher apnea-hypopnea index (P<0.001) and apnea-

hypopnea-related arousal index (P<0.001) as compared with non-asthmatics. Deep sleep was decreased in asthmatics (P=0.001). In the vigilance test, the mean number of correct answers was lower (P=0.005) and the mean reaction time was slower (P=0.002) in asthmatic children. A hierarchical multiple linear regression showed that deep sleep and apnea-hypopnea-related arousal index were significant predictors of vigilance. The data suggest that the prevalence of paediatric sleep-disordered breathing and sleep fragmentation could be very high among children with well-controlled asthma. Moreover, vigilance, the ability to maintain attention and alertness, was worse in stable asthmatic children when compared with healthy controls. Sleep-disordered breathing should be checked even in stable asthmatic children as they are at risk for developing neurobehavioural deterioration associated with frequent arousals during sleep. Furthermore, early treatment for asthma may be required in order to prevent airway remodelling that could cause sleep problems.

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#### J Am Acad Child Adolesc Psychiatry. 2014;53:351-61.

# ABNORMAL AMYGDALA FUNCTIONAL CONNECTIVITY ASSOCIATED WITH EMOTIONAL LABILITY IN CHILDREN WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.

#### Hulvershorn LA, Mennes M, Castellanos FX, et al.

**Objective** A substantial proportion of children with attention-deficit/ hyperactivity disorder (ADHD) also display emotion regulation deficits manifesting as chronic irritability, severe temper outbursts, and aggression. The amygdala is implicated in emotion regulation, but its connectivity and relation to emotion regulation in ADHD has yet to be explored. The purpose of this study was to examine the relationship between intrinsic functional connectivity (iFC) of amygdala circuits and emotion regulation deficits in youth with ADHD.

**Method** Bilateral amygdala iFC was examined using functional magnetic resonance imaging in 63 children with ADHD, aged 6 to 13 years. First, we examined the relationship between amygdala IFC and parent ratings of emotional lability (EL) in children with ADHD. Second, we compared amygdala iFC across subgroups of children with ADHD and high EL (n=18), ADHD and low EL (n=20), and typically developing children (TDC), all with low EL (n=19).

**Results** Higher EL ratings were associated with greater positive iFC between the amygdala and rostral anterior cingulate cortex in youth with ADHD. EL scores were also negatively associated with iFC between bilateral amygdala and posterior insula/superior temporal gyrus. Patterns of amygdala-cortical iFC in ADHD participants with low EL were not different from the comparison group, and the effect sizes for these comparisons were smaller than those for the trend-level differences observed between the high-EL and TDC groups.

**Conclusions** In children with ADHD and a range of EL, deficits in emotion regulation were associated with altered amygdala-cortical iFC. When comparing groups that differed on ADHD status but not EL, differences in amygdala iFC were small and nonsignificant, highlighting the specificity of this finding to emotional deficits, independent of other ADHD symptoms.

BESONDERHEITEN IN DER MULTIAXIALEN KLASSIFIZIERUNG, ANAMNESE UND PSYCHOPATHOLOGIE BEI KINDERN UND JUGENDLICHEN MIT EINER AUTISMUS-SPEKTRUM- STÖRUNG UND EINER AUFMERKSAMKEITSDEFIZIT-/ HYPERAKTIVITÄTSSTÖRUNG.

Sinzig J, Vinzelberg I, Bell H, et al.

The aim of the current study was to compare the ICD-10 multiaxial classification scheme (MAS), developmental history, and psychopathology in children with autism spectrum disorder (ASD) with or without attention-deficit/hyperactivity disorder (ADHD. A total of 120 patients were included in the study (ASD: n=60; ASD + ADHD: n=60). Data were obtained from each child's developmental history, family history, the MAS, and diagnostic measures (MBAS, FSK, SRS, CBCL). In the group ASD + ADHD, mothers consumed more toxic substances during pregnancy than in the ASD group. In both ASD and ASD+ADHD, fathers tended to be employed in an academic or technical setting. In the questionnaires an increased rate of external psychopathological symptoms was found in ASD + ADHD. In summary, patients with ASD and comorbid ADHS demonstrated a higher rate of comorbid psychopathology than reported in previous studies. This result should be taken into account in diagnostics and therapy.

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Ky Nurse. 2014 Jan;62:5-6. COMPLEMENTARY TREATMENT OPTIONS FOR CHILDHOOD AND ADOLESCENT ATTENTION DEFICIT/HYPERACTIVITY DISORDER. Costelle D.

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N Engl J Med. 2014 Feb;370:838-46.

CLINICAL PRACTICE. ATTENTION DEFICIT-HYPERACTIVITY DISORDER IN CHILDREN AND ADOLESCENTS. *Feldman HM, Reiff MI.* 

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Neurochem Res. 2014.

POTENTIAL CONTRIBUTION OF MONOAMINE OXIDASE A GENE VARIANTS IN ADHD AND BEHAVIORAL CO-MORBIDITIES: SCENARIO IN EASTERN INDIAN PROBANDS.

#### Karmakar A, Maitra S, Verma D, et al.

Attention deficit hyperactivity disorder (ADHD) is the most frequently diagnosed behavioral disorder in children with a high frequency of co-morbid conditions like conduct disorder (CD) and oppositional defiant disorder (ODD). These traits are controlled by neurotransmitters like dopamine, serotonin and norepinephrine. Monoamine oxidase A (MAOA), a mitochondrial enzyme involved in the degradation of amines, has been reported to be associated with aggression, impulsivity, depression, and mood changes. We hypothesized that MAOA can have a potential role in ADHD associated CD/ODD and analyzed 24 markers in a group of Indo-Caucasoid subjects. ADHD probands and controls (N=150 each) matched for ethnicity and gender were recruited following the Diagnostic and Statistical Manual for Mental Disorders-IV. Appropriate scales were used for measuring CD and ODD traits. Markers were genotyped by PCR-based methods and data obtained analyzed using the Cocaphase program under UNPHASED. Only eight markers were found to be polymorphic. rs6323 "G" allele showed higher frequencies in ADHD (P=0.0023), ADHD + CD (P=0.03) and ADHD + ODD (P=0.01) as

compared to controls. Haplotype analysis revealed statistically significant difference for three haplotypes in ADHD cases (P<0.02). Statistically significant differences were also noticed for haplotypes in ADHD + CD and ADHD + ODD cases (P<0.01). LD analysis showed significant variation in different groups. Multidimensionality reduction analysis showed independent as well as interactive effects of markers. Genotypes showed correlation with behavioral problems in ADHD and ADHD + CD. We interpret that MAOA gene variants may contribute to the etiology of ADHD as well as associated co-morbid CD and ODD in this ethnic group.

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#### Neuropsychologia. 2014;56:178-83.

# INFLUENCE OF METHYLPHENIDATE ON SPATIAL ATTENTION ASYMMETRY IN ADOLESCENTS WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER (ADHD): PRELIMINARY FINDINGS. Silk TJ, Newman DP, Eramudugolla R, et al.

Atypical asymmetries of spatial attention have been reported in children with attention deficit hyperactivity disorder (ADHD) and may be exacerbated by non-spatial factors such as attentional capacity. Although preliminary evidence suggests that asymmetries of attention in ADHD may be modifiable by the psychostimulant, methylphenidate, further placebo-controlled studies are required. This study first aimed to confirm recent evidence that increasing non-spatial processing load at fixation can unmask a spatial gradient of target detection in children with ADHD but not Controls. Second, we used placebo-controlled randomised trial methodology to ask whether 20. mg of methylphenidate (MPH) could remediate any load-dependent asymmetry of spatial attention in adolescents with ADHD. Twelve male adolescents with ADHD were assessed twice in a double-blind, randomized design, under either placebo or an acute dose of methylphenidate. Thirteen typically developing adolescent Controls completed a single session under placebo. Participants completed a computer-based task in which they monitored a centrally presented rapid serial visual presentation stream for a probe stimulus, while also responding to brief peripheral events. The attentional load of the central task was manipulated by varying the target instructions but not the physical stimuli or the frequency of targets. Between-group analyses under placebo conditions indicated that increased attentional load induced a spatial gradient for target detection in the ADHD but not Controls, such that load slowed response times for left, but not, right hemi-field targets. This load-dependent spatial asymmetry in the adolescents with ADHD was abolished by administration of methylphenidate. Methylphenidate may "normalise" target detection between the hemi-fields in ADHD via enhancement of the right-lateralised ventral attention networks that support non-spatial attention.

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Neuropsychology. 2014.

# WORKING MEMORY AND INTRAINDIVIDUAL VARIABILITY AS NEUROCOGNITIVE INDICATORS IN ADHD: EXAMINING COMPETING MODEL PREDICTIONS.

#### Kofler MJ, Alderson RM, Raiker JS, et al.

**Objective**: The current study examined competing predictions of the default mode, cognitive neuroenergetic, and functional working memory models of attention-deficit/hyperactivity disorder (ADHD) regarding the relation between neurocognitive impairments in working memory and intraindividual variability.

**Method**: Twenty-two children with ADHD and 15 typically developing children were assessed on multiple tasks measuring intraindividual reaction time (RT) variability (ex-Gaussian: tau, sigma) and central executive (CE) working memory. Latent factor scores based on multiple,

counterbalanced tasks were created for each construct of interest (CE, tau, sigma) to reflect reliable variance associated with each construct and remove task-specific, test-retest, and random error.

**Results**: Bias-corrected, bootstrapped mediation analyses revealed that CE working memory accounted for 88% to 100% of ADHD-related RT variability across models, and between-group differences in RT variability were no longer detectable after accounting for the mediating role of CE working memory. In contrast, RT variability accounted for 10% to 29% of between-group differences in CE working memory, and large magnitude CE working memory deficits remained after accounting for this partial mediation. Statistical comparison of effect size estimates across models suggests directionality of effects, such that the mediation effects of CE working memory on RT variability were significantly greater than the mediation effects of RT variability on CE working memory.

**Conclusions**: The current findings question the role of RT variability as a primary neurocognitive indicator in ADHD and suggest that ADHD-related RT variability may be secondary to underlying deficits in CE working memory.

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#### Neuropsychology. 2014;28:202-11.

## CONTINUOUS PERFORMANCE TEST II OUTCOMES IN 11-YEAR-OLD CHILDREN WITH EARLY ADHD SYMPTOMS: A LONGITUDINAL STUDY.

#### Lopez-Vicente M, Sunyer J, Forns J, et al.

**Objective**: This study aimed to assess the association between attention-deficit hyperactivity disorder (ADHD) symptoms at preschool age and attention functioning at 11 years old.

**Method**: Four-year-old children (n=422) were assessed using the Diagnostic and Statistical Manual of Mental Disorders (4th ed.; American Psychiatric Association, 1994) ADHD form list for inattention and hyperactivity symptoms. Cognitive development and social behavior were also assessed at this age. The Continuous Performance Test II (CPT-II) was used to assess attention function when the children were 11 years old.

**Results**: The presence of inattention symptoms predicted more omission errors (incidence rate ratio [IRR] = 1.07, 95% CI [1.02, 1.12]) and slower hit reaction time (HRT; (beta)=3.27, 95% CI [0.72, 5.81]) in CPT-II. Both inattention and hyperactivity symptoms predicted greater standard error in the HRT (HRT [SE]) (IRR=1.02, 95% CI [1.01, 1.03]). The inclusion of social competence and cognitive scores in the multivariate regression models diminished the association with omissions, whereas their inclusion did not change associations with the two HRT outcomes. Stronger associations between inattention symptoms and HRT were observed in the last 2 time-duration blocks of the CPT-II. No associations were found with commissions and detectability.

**Conclusions**: The presence of ADHD symptoms in preschool children was longitudinally associated with a lower performance on the CPT-II. Omission errors seemed to be partly explained by early social and cognitive competences. Slower HRTs showed a direct association with inattention symptoms, particularly in the latest CPT-II blocks. HRT (SE) was strongly related to hyperactivity symptoms.

#### Neurotoxicol Teratol. 2014;42:43-50.

# CORRESPONDENCE OF PARENT REPORT AND LABORATORY MEASURES OF INATTENTION AND HYPERACTIVITY IN CHILDREN WITH HEAVY PRENATAL ALCOHOL EXPOSURE.

#### Glass L, Graham DM, Deweese BN, et al.

Clinical research and practice support a multi-method approach to validating behavioral problems in children. We examined whether parent-reported symptoms of hyperactivity and inattention (using the Disruptive Behavior Disorder Rating Scale) were substantiated by objective laboratory measures [hyperactivity measured by wrist-worn actigraphy (ACT) and inattention assessed using a 20-minute continuous performance task (CPT)] in three age- and demographicallymatched groups of school-age children: children with prenatal alcohol exposure (AE), nonexposed children with idiopathic ADHD (ADHD), and controls (CON). Results indicated that the clinical groups (AE, ADHD) had significantly higher parent-reported levels for both domains compared to the CON group, and did not differ from each other. On the laboratory measures, the clinical groups were more inattentive than controls on the CPT, but did not differ from each other. In contrast, the ADHD group had higher objective activity on the ACT than AE and CON, which did not differ from each other. Thus, laboratory measures differentially validated parent reports in a group-dependent manner. Actigraphy substantiated parent-reported hyperactivity for children in the ADHD group but not for children in the AE group, while the CPT validated parent-reported inattention for both clinical groups. Although the majority of children in the AE group met the criteria for ADHD, objective activity levels were not different from controls, indicating that hyperactivity may be a less prominent feature in the AE group. Thus, while there is considerable overlap between the effects of prenatal alcohol exposure and ADHD, differences in behavioral profiles may be clinically useful in differential diagnosis. Further, these data indicate that objective measures should be used to validate parent reports.

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#### New Engl J Med. 2014;370:838-46. ATTENTION DEFICIT-HYPERACTIVITY DISORDER IN CHILDREN AND ADOLESCENTS. Feldman HM, Reiff MI.

A 9-year-old boy who received a diagnosis of attention deficit- hyperactivity disorder (ADHD) at 7 years of age is brought to your office by his parents for a follow-up visit. He had had behavioral problems since preschool, including excessive fidgeting and difficulty following directions and taking turns with peers. Parent and teacher ratings of behavior confirmed elevated levels of inattention, hyperactivity, and impulsivity that were associated with poor grades, disruptions of classroom activities, and poor peer relationships. He was treated with sustained-release methylphenidate. Although parent and teacher rating scales after treatment showed reduced symptoms, he still makes many careless mistakes and has poor grades and no friends. What would you advise?

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Paediatr Anaesth. 2014.

EXPOSURE TO GENERAL ANESTHESIA IN EARLY LIFE AND THE RISK OF ATTENTION DEFICIT/HYPERACTIVITY DISORDER DEVELOPMENT: A NATIONWIDE, RETROSPECTIVE MATCHED-COHORT STUDY.

#### Ko WR, Liaw YP, Huang JY, et al.

**Background**: Postnatal exposure to anesthetics can cause neural apoptosis and degeneration in animals, but results from studies conducted on humans were discordant. Previous studies

contained no information on the relationship between neurobehavioural disorders and anesthesia exposure in Asian children. We conducted a retrospective matched-cohort study in Taiwan to investigate the association of early life anesthesia exposure with risk of attention deficit/hyperactivity disorder (ADHD).

**Methods**: Data were obtained from the National Health Insurance Research Database of Taiwan. Children born between January 1, 2001 and December 31, 2005 were included. Each child with anesthesia exposure before 3 years of age was matched to four unexposed children. Observation was concluded on December 31, 2010. Proportional hazards regression was used to assess the association of anesthesia exposure with ADHD. Analyses were also made based on exposure number and age at the time of first exposure.

**Results**: This matched-cohort comprised of 16 465 children, among which 3293 were exposed to general anesthesia before age 3 years. The adjusted hazard ratio of developing ADHD was 1.06 (95% CI: 0.86,1.31) for general anesthesia exposure. The adjusted hazard ratio of developing ADHD for single and multiple exposures were 1.11 (95% CI: 0.88, 1.41) and 0.96 (95% CI: 0.71,1.31), respectively. No trend of increasing risk was noted based on age at the time of first exposure.

**Conclusions**: Exposure to general anesthesia before 3 years of age was not associated with ADHD.

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#### Pediatr Rep. 2013;5:76-80.

EARLY PRECURSORS OF LOW ATTENTION AND HYPERACTIVITY IN MODERATELY AND VERY PRETERM CHILDREN AT PRESCHOOL AGE.

#### Morales MR, Polizzi C, Sulliotti G, et al.

The low attention and hyperactivity are major morbidities associated with very and moderately preterm birth. The study has been aimed at investigating the likely occurrence of early precursors of Attention Deficit and Hyperactivity Disorder (ADHD) in very and moderately preterm children at preschool age. The involved children were: 25 very preterm children (M=29.4 weeks of gestational age, SD=2), with low birth weight (M=1200 g, SD=250 g); 35 moderately preterm children (M=34.6 weeks of gestational age, SD=1) with low birth weight (M=2100 g, SD=250 g); 60 healthy full-term children as the control group. Parents of children have been administered specific questionnaires to detect low attention and hyperactivity of their children at home. The data have shown the risk of precursors of ADHD, highlighting statistically significant birth-related differences in both hyperactivity/impulsivity [F(2,119)=3.5, P=0.03, (eta)2=0.06] and inattention [F(2,119)=2.4, P=0.04, (eta)2=0.04], where very preterm children have got higher scores in these two dimensions compared with full-term and moderately preterm children. The very preterm children have got higher scores of impulsivity and inattention than the full-term children (Tukey'HSD - Honestly Significant Difference; P<0.001).

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#### Pediatrics. 2014;133:483-92.

IN-SCHOOL NEUROFEEDBACK TRAINING FOR ADHD: SUSTAINED IMPROVEMENTS FROM A RANDOMIZED CONTROL TRIAL.

#### Steiner NJ, Frenette EC, Rene KM, et al.

**OBJECTIVE**: To evaluate sustained improvements 6 months after a 40-session, in-school computer attention training intervention using neurofeedback or cognitive training (CT) administered to 7- to 11- year-olds with attention-deficit/hyperactivity disorder (ADHD).

**METHODS**: One hundred four children were randomly assigned to receive neurofeedback, CT, or a control condition and were evaluated 6 months postintervention. A 3-point growth model assessed change over time across the conditions on the Conners 3-Parent Assessment Report (Conners 3-P), the Behavior Rating Inventory of Executive Function Parent Form (BRIEF), and a systematic double-blinded classroom observation (Behavioral Observation of Students in Schools). Analysis of variance assessed community-initiated changes in stimulant medication.

**RESULTS**: Parent response rates were 90% at the 6-month follow-up. Six months postintervention, neurofeedback participants maintained significant gains on Conners 3-P (Inattention effect size [ES]=0.34, Executive Functioning ES=0.25, Hyperactivity/Impulsivity ES=0.23) and BRIEF subscales including the Global Executive Composite (ES=0.31), which remained significantly greater than gains found among children in CT and control conditions. Children in the CT condition showed delayed improvement over immediate postintervention ratings only on Conners 3-P Executive Functioning (ES=0.18) and 2 BRIEF subscales. At the 6-month follow-up, neurofeedback participants maintained the same stimulant medication dosage, whereas participants in both CT and control conditions showed statistically and clinically significant increases (9 mg [P=.002] and 13 mg [P<.001], respectively).

**CONCLUSIONS**: Neurofeedback participants made more prompt and greater improvements in ADHD symptoms, which were sustained at the 6-month follow-up, than did CT participants or those in the control group. This finding suggests that neurofeedback is a promising attention training treatment for children with ADHD.

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### PLoS One. 2014 Mar 13;9(3):e90744.

## A SCOPING REVIEW OF INTERVENTIONS TO SUPPLEMENT SPOKEN COMMUNICATION FOR CHILDREN WITH LIMITED SPEECH OR LANGUAGE SKILLS.

## Costantino MA, Bonati M.

**BACKGROUND**: Augmentative and Alternative Communication (AAC) is used for treating children with severe disorders of speech-language production and/or comprehension. Various strategies are used, but research and debate on their efficacy have remained limited to a specific area and have rarely reached the general medical community.

**OBJECTIVE**: To systematically evaluate outcomes of AAC interventions in children with limited speech or language skills.

**METHODS**: Searches were conducted (up to December 2012) in the MEDLINE, EMBASE, PsycINFO, CINAHL, DARE, and Cochrane Library databases. Furthermore, relevant journals were searched by hand. References from identified studies were examined. Only RCTs were considered. Trial quality was assessed according to a standardized and validated set of criteria.

**RESULTS**: Fourteen of 1661 retrieved papers met inclusion criteria. A total of 666 children were included in the review and 7 papers involved only children <5 years old. Papers were of average quality and all but one had been published during the previous 10 years by one of 8 research groups, 5 of which from the United States. Seven studies directly addressed AAC use by children with different disabilities. Seven studies enrolled typically developing children: 5 evaluated the use of AAC technologies by children without disabilities in order to obtain results that could be used to improve interventions in peers with disabilities, and 2 evaluated peers' attitudes towards children who used AAC. Both interventions and outcome measures varied widely between studies. Overall findings demonstrate the effectiveness of the AAC interventions considered, but the focus on RCTs alone appears too restrictive.

**CONCLUSIONS**: Solid evidence of the positive effects of AAC interventions in children with severe communication disorders must be generated, and different methods are needed besides

RCTs. Moreover, it is important that knowledge, research, and debate extend to the medical community in order to ensure clinically effective AAC provision for these children (and their parents).

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## PLoS ONE. 2013;8.

EXTREME LEARNING MACHINE-BASED CLASSIFICATION OF ADHD USING BRAIN STRUCTURAL MRI DATA.

## Peng X, Lin P, Zhang T, et al.

**Background**: Effective and accurate diagnosis of attention-deficit/ hyperactivity disorder (ADHD) is currently of significant interest. ADHD has been associated with multiple cortical features from structural MRI data. However, most existing learning algorithms for ADHD identification contain obvious defects, such as time-consuming training, parameters selection, etc.

**The aims** of this study were as follows: (1) Propose an ADHD classification model using the extreme learning machine (ELM) algorithm for automatic, efficient and objective clinical ADHD diagnosis. (2) Assess the computational efficiency and the effect of sample size on both ELM and support vector machine (SVM) methods and analyze which brain segments are involved in ADHD.

**Methods**: High-resolution three-dimensional MR images were acquired from 55 ADHD subjects and 55 healthy controls. Multiple brain measures (cortical thickness, etc.) were calculated using a fully automated procedure in the FreeSurfer software package. In total, 340 cortical features were automatically extracted from 68 brain segments with 5 basic cortical features. F-score and SFS methods were adopted to select the optimal features for ADHD classification. Both ELM and SVM were evaluated for classification accuracy using leave-one-out cross-validation.

**Results**: We achieved ADHD prediction accuracies of 90.18% for ELM using eleven combined features, 84.73% for SVM-Linear and 86.55% for SVM-RBF. Our results show that ELM has better computational efficiency and is more robust as sample size changes than is SVM for ADHD classification. The most pronounced differences between ADHD and healthy subjects were observed in the frontal lobe, temporal lobe, occipital lobe and insular.

**Conclusion**: Our ELM-based algorithm for ADHD diagnosis performs considerably better than the traditional SVM algorithm. This result suggests that ELM may be used for the clinical diagnosis of ADHD and the investigation of different brain diseases.

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## PLoS ONE. 2014;9.

VISUAL PROCESSING OF BIOLOGICAL MOTION IN CHILDREN AND ADOLESCENTS WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER: AN EVENT RELATED POTENTIAL-STUDY.

## Kroger A, Hof K, Krick C, et al.

Attention-deficit/hyperactivity disorder (ADHD) is often accompanied by problems in social behaviour, which are sometimes similar to some symptoms of autism-spectrum disorders (ASD). However, neuronal mechanisms of ASD-like deficits in ADHD have rarely been studied. The processing of biological motion-recently discussed as a marker of social cognition-was found to be disrupted in ASD in several studies. Thus in the present study we tested if biological motion processing is disrupted in ADHD. We used 64-channel EEG and spatio-temporal source analysis to assess event-related potentials associated with human motion processing in 21 children and adolescents with ADHD and 21 matched typically developing controls. On the behavioural level, all subjects were able to differentiate between human and scrambled motion. But in response to

both scrambled and biological motion, the N200 amplitude was decreased in subjects with ADHD. After a spatio-temporal dipole analysis, a human motion specific activation was observable in occipital-temporal regions with a reduced and more diffuse activation in ADHD subjects. These results point towards neuronal determined alterations in the processing of biological motion in ADHD.

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### Postgrad Med. 2014 Jan;126:153-77.

## LOW DOPAMINE FUNCTION IN ATTENTION DEFICIT/HYPERACTIVITY DISORDER: SHOULD GENOTYPING SIGNIFY EARLY DIAGNOSIS IN CHILDREN?

## Gold MS, Blum K, Oscar-Berman M, et al.

Attention deficit/hyperactivity disorder (ADHD) is present in 8% to 12% of children, and 4% of adults worldwide. Children with ADHD can have learning impairments, poor selfesteem, social dysfunction, and an increased risk of substance abuse, including cigarette smoking. Overall, the rate of treatment with medication for patients with ADHD has been increasing since 2008, with >/= 2 million children now being treated with stimulants. The rise of adolescent prescription ADHD medication abuse has occurred along with a concomitant increase of stimulant medication availability. Of adults presenting with a substance use disorder (SUD), 20% to 30% have concurrent ADHD, and 20% to 40% of adults with ADHD have a history of SUD. Following a brief review of the etiology of ADHD, its diagnosis and treatment, we focus on the benefits of early and appropriate testing for a predisposition to ADHD. We suggest that by genotyping patients for a number of known, associated dopaminergic polymorphisms, especially at an early age, misdiagnoses and/or over-diagnosis can be reduced. Ethical and legal issues of early genotyping are considered. As many as 30% of individuals with ADHD are estimated to either have secondary side-effects or are not responsive to stimulant medication. We also consider the benefits of non-stimulant medication and alternative treatment modalities, which include diet, herbal medications, iron supplementation, and neurofeedback. With the goals of improving treatment of patients with ADHD and SUD prevention, we encourage further work in both genetic diagnosis and novel treatment approaches.

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Prog Neuro-Psychopharmacol Biol Psychiatry. 2014.

## **ADHD**, ALTERED DOPAMINE NEUROTRANSMISSION, AND DISRUPTED REINFORCEMENT PROCESSES: IMPLICATIONS FOR SMOKING AND NICOTINE DEPENDENCE.

## Kollins SH, Adcock RA.

Attention deficit hyperactivity disorder (ADHD) is a common and impairing disorder affecting millions of children, adolescents, and adults. Individuals with ADHD smoke cigarettes at rates significantly higher than their non-diagnosed peers and the disorder also confers risk for a number of related adverse smoking outcomes including earlier age of initiation, faster progression to regular use, heavier smoking/greater dependence, and more difficulty quitting. Progress in our understanding of dopamine neurotransmission and basic behavioral reinforcement processes in ADHD may help increase our understanding of the ADHD-smoking comorbidity. This review will examine how these areas have been studied and how further work may aid in the development of better prevention and treatment for smoking in those with ADHD.

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## Psychiatr Q. 2014;85:103-10.

## ATTENTION PROBLEMS AND PATHOLOGICAL GAMING: RESOLVING THE 'CHICKEN AND EGG' IN A PROSPECTIVE ANALYSIS.

## Ferguson CJ, Ceranoglu TA.

Pathological gaming (PG) behaviors are behaviors which interfere with other life responsibilities. Continued debate exists regarding whether symptoms of PG behaviors are a unique phenomenon or arise from other mental health problems, including attention problems. Development of attention problems and occurrence of pathological gaming in 144 adolescents were followed during a 1-year prospective analysis. Teens and their parents reported on pathological gaming behaviors, attention problems, and current grade point average, as well as several social variables. Results were analyzed using regression and path analysis. Attention problems tended to precede pathological gaming predicted lower GPA 1 year later. Current results suggest that pathological gaming arises from attention problems, but not the inverse. These results suggest that pathological gaming behaviors are symptomatic of underlying attention related mental health issues, rather than a unique phenomenon.

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#### Psychiatry Clin Neurosci. 2014.

PARENTAL QUALITY OF LIFE AND DEPRESSIVE MOOD FOLLOWING METHYLPHENIDATE TREATMENT OF CHILDREN WITH ATTENTION-DEFICIT HYPERACTIVITY DISORDER.

## Kim Y, Kim B, Chang JS, et al.

**Aim**: This naturalistic study investigated the associations between quality of life and depressive mood in parents and symptom changes in attention-deficit hyperactivity disorder (ADHD) children.

**Methods**: At baseline and at weeks 4 and 8, the parents evaluated their children, who were receiving treatment with osmotic-release oral system methylphenidate (mean dosage 36.3(plus or minus)15.5mg/day), using the Swanson, Nolan, and Pelham - Fourth Edition (SNAP-IV-18) scale. The parents evaluated themselves using the Beck Depression Inventory (BDI) and the World Health Organization Quality of Life Assessment, Brief Version (WHOQOL-BREF).

**Results**: A significant reduction in SNAP-IV-18 scores and improvements in parental BDI scores and parental WHOQOL-BREF scores were observed. The decrease in BDI scores from baseline to 8 weeks was significantly associated with increases in WHOQOL-BREF sub-domain scores from baseline to 8 weeks, with a greater decrease at 4 weeks and after. The decrease in the SNAP-IV-18 hyperactivity-impulsivity score was significantly associated with increases in WHOQOL social sub-domain scores from baseline to 8 weeks. For those patients who showed a 25% or greater decrease in the SNAP-IV-18 total scores from baseline to 8 weeks, the decreases in the SNAP-IV-18 total score and in the inattention and hyperactivity-impulsivity scores were significantly associated with a decrease in BDI scores from baseline to 8 weeks.

**Conclusion**: Methylphenidate treatment for ADHD was associated with both symptom alleviation in children with ADHD and improvement in parental depressive mood and quality of life, suggesting that the effects of treatment could go beyond symptom improvement in ADHD.

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## Psychiatry Res. 2014.

## DISTINGUISHING BORDERLINE PERSONALITY DISORDER FROM ADULT ATTENTION DEFICIT/HYPERACTIVITY DISORDER: A CLINICAL AND DIMENSIONAL PERSPECTIVE. *Prada P, Hasler R, Baud P, et al.*

Adult attention deficit hyperactivity disorder (ADHD) is frequently associated with borderline personality disorder (BPD). As both disorders share some core clinical features they are sometimes difficult to distinguish from one another. The present work aimed to investigate differences in the expression of impulsivity, anger and aggression, quality of life as well as the number and severity of the comorbidities between ADHD, BPD, comorbid BPD-ADHD and control subjects. ADHD and BPD-ADHD patients showed a higher level of impulsivity than BPD and control subjects. BPD-ADHD patients had higher levels of substance abuse/dependence and higher levels of aggression than the other groups. Comorbid BPD-ADHD patients showed high levels of impulsivity and aggression, a characteristic that should draw the attention of clinicians on the necessity of providing an accurate diagnosis. The question also arises as to whether they represent a distinct clinical subgroup with specific clinical characteristics, outcomes and vulnerability factors.

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### Psychiatry Res. 2014.

RESTING ELECTROENCEPHALOGRAM IN ATTENTION DEFICIT HYPERACTIVITY DISORDER: DEVELOPMENTAL COURSE AND DIAGNOSTIC VALUE.

## Buyck I, Wiersema JR.

This study investigated electroencephalographic (EEG) activity and its developmental course in attention deficit hyperactivity disorder (ADHD) throughout the lifespan, as well as the accuracy of EEG parameters in distinguishing ADHD patients from typically developing individuals. Three minutes eyes closed resting EEG was compared between 62 individuals with ADHD (36 children, 26 adults) and 55 typically developing individuals (30 children, 25 adults). EEG activity and maturation did not differ between individuals with ADHD and typically developing individuals. However, despite comparable developmental course between clinical groups, persistent elevated theta/beta ratio and reduced relative beta power were observed in the ADHD inattentive subtype compared to the ADHD combined subtype and controls across the lifespan. Therefore, a maturational deviation rather than a maturational delay may underlie a subgroup of ADHD. EEG based classification failed for ADHD but proved successful for age. These findings emphasize heterogeneity in ADHD throughout the lifespan and question clinical utility of conventional EEG approaches for diagnostic purposes in ADHD.

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## Psychol Assess. 2014;26:195-206.

DIFFERENTIATING BIPOLAR DISORDER FROM UNIPOLAR DEPRESSION AND ADHD: THE UTILITY OF THE GENERAL BEHAVIOR INVENTORY.

### Pendergast LL, Youngstrom EA, Merkitch KG, et al.

Adolescence and early adulthood are the peak ages for the onset of unipolar and bipolar mood disorders. Moreover, for most individuals with attention-deficit/hyperactivity disorder (ADHD), symptoms and impairment begin in childhood but persist well into adolescence and adulthood (e.g., Barkley, 2010). Thus, adolescence and early adulthood represent a developmental window wherein individuals can be affected by mood disorders, ADHD, or both. Because treatment protocols for unipolar depression (UPD), bipolar disorder (BD), and ADHD are quite different, it is

crucial that assessment instruments used among adolescents and young adults differentiate between these disorders. The primary objectives of this study were to evaluate the predictive and diagnostic validity of General Behavior Inventory (GBI; Depue et al., 1981) scores in discriminating BD from UPD and ADHD. Participants were drawn from adolescent (n=361) and young adult (n=614) samples. Based on findings from logistic regression and receiver-operating characteristics analyses, the diagnostic efficiency of the GBI scales range from fair (discriminating UPD from BD) to good (discriminating BD participants from nonclinical controls). Multilevel diagnostic likelihood ratios are also provided to facilitate individual decision making.

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## Psychopharmacology. 2014;1-11.

## DIFFERENTIAL RESPONSES OF TWO RELATED NEUROSTEROIDS TO METHYLPHENIDATE BASED ON ADHD SUBTYPE AND THE PRESENCE OF DEPRESSIVE SYMPTOMATOLOGY.

## Molina-Carballo A, Justicia-Martinez F, Moreno-Madrid F, et al.

**Rationale**: Attention deficit with hyperactivity disorder is a neurodevelopmental disorder associated with alterations in the prefrontal cortex via dopaminergic and noradrenergic neurotransmission. Neurosteroids (e.g. allopregnanolone and dehydroepiandrosterone) modulate the release of multiple neurotransmitters.

**Objective**: This study aims to determine the baseline concentrations and daily variations in allopregnanolone and dehydroepiandrosterone in children with attention deficit hyperactivity disorder (ADHD) and to determine the effect of chronic administration of methylphenidate on clinical symptoms and on the concentrations of these two neurosteroids.

**Methods**: We included 148 children aged 5 to 14 years, subdivided into two groups: ADHD group (n=107, with a diagnosis of ADHD (DSM-IV-TR criteria), further classified in subtypes by an "attention deficit and hyperactivity scale" and subgroups by the "Children's Depression Inventory") and a control group (n=41). The clinical workup included blood samples that were drawn at 20:00 and 09:00 hours, at inclusion in both groups, and after 4.61 (plus or minus) 2.29 months of treatment only in the ADHD group, for measurements for allopregnanolone and dehydroepiandrosterone. Factorial analysis, adjusted for age and gender, was performed by using Stata 12.0.

**Results**: Methylphenidate induced the doubling of allopregnanolone levels in the predominantly inattentive ADHD patients without depressive symptoms (27.26 (plus or minus) 12.90 vs. 12.67 (plus or minus) 6.22 ng/ml, morning values). Although without statistical differences, baseline dehydroepiandrosterone levels were higher and slightly increased after methylphenidate in the ADHD subtype with depressive symptoms (7.74 (plus or minus) 11.46 vs. 6.18 (plus or minus) 5.99 ng/ml, in the morning), opposite to the lower baseline levels, and further decrease after methylphenidate in the inattentive subtype with depressive symptoms.

**Conclusions**: Different neurosteroids may have different baseline concentrations and differential responses to methylphenidate treatment as a function of ADHD subtype and subgroup. These differential responses may be a clinical marker of ADHD subtype and/or co-morbidities.

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Psychotherapy. 2014 Mar;51:110-16.

## STRUCTURED DYADIC BEHAVIOR THERAPY PROCESSES FOR ADHD INTERVENTION. *Curtis DF.*

Children with Attention-Deficit/Hyperactivity Disorder (ADHD) present significant problems with behavioral disinhibition that often negatively affect their peer relationships. Although behavior

therapies for ADHD have traditionally aimed to help parents and teachers better manage children's ADHD-related behaviors, therapy processes seldom use peer relationships to implement evidence-based behavioral principles. This article introduces Structured Dyadic Behavior Therapy as a milieu for introducing effective behavioral techniques within a socially meaningful context. Establishing collaborative behavioral goals, benchmarking, and redirection strategies are discussed to highlight how in-session dyadic processes can be used to promote more meaningful reinforcement and change for children with ADHD. Implications for improving patient care, access to care, and therapist training are also discussed.

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Res Dev Disabil. 2014.

## COMMONLY STUDIED COMORBID PSYCHOPATHOLOGIES AMONG PERSONS WITH AUTISM SPECTRUM DISORDER.

## Matson JL, Cervantes PE.

The study of comorbid psychopathology among persons with autism spectrum disorder (ASD) is picking up steam. The purpose of this paper was to review and describe important characteristics of existing studies. Among the current crop of papers, depression, anxiety, and attention-deficit/hyperactivity disorder (ADHD) have been frequently evaluated. Groups studied have most frequently been children. Persons with ASD and normal intelligence quotient (IQ) scores have been studied more often than individuals with ASD and intellectual disability. Additional characteristics are discussed, and the implications of these data for future developments in the field are reviewed.

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Revista Brasileira de Psiquiatria. 2014;36:53-59.

DOES COMORBID BIPOLAR DISORDER INCREASE NEUROPSYCHOLOGICAL IMPAIRMENT IN CHILDREN AND ADOLESCENTS WITH ADHD?

## Narvaez JC, Zeni CP, Coelho RP, et al.

**Objective**: To assess differences in executive functioning between children and adolescents with attention-deficit/hyperactivity disorder (ADHD) comorbid or not with bipolar disorder (BD), and to study the neuropsychological profile of subjects with the comorbidity in a clinical sample from a developing country.

**Method**: Case-control study comparing 23 participants with BD + ADHD and 85 ADHD-only subjects aged 6 to 17 years old. Both groups were drug-free. Executive function domains were assessed with the Stroop Test, the Wisconsin Card Sorting Test, and the Continuous Performance Test II.

**Results**: The group with juvenile BD + ADHD showed a significantly worse performance on the Stroop task, including time in color (p=0.002), time in color-word (p, 0.001), interference, number or errors in color and color-word (p=0.001), and number of errors in word cards (p = 0.028). No between-group differences were found in other tests.

**Conclusions**: Our findings suggest that ADHD-only and ADHD + BD do not show differences in inhibitory control and set-shifting domains. However, children and adolescents with BD and comorbid ADHD show greater impairment in processing speed and interference control. This suggests a potentially higher impairment in the dorsolateral prefrontal cortex and may be a potential neuropsychological signature of juvenile BD comorbid with ADHD.

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Rev Neurol. 2014;58:S107-S110.

## ORALITY AND WRITING: ARGUMENTATION IN CHILDREN WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER.

## Gallardo-Pauls B, Moreno-Campos V.

**Introduction**. This work takes a deeper look at the differences in the linguistic competence of children with attention deficit hyperactivity disorder (ADHD) in terms of both orality and writing.

**Aims**. The purpose of this study is to check whether, in oral tasks, these children present the same problems related to inhibition and self-regulation as those pointed out in research working with written data. Likewise it seeks to describe those problems (lack of appropriateness, inappropriate production) as they appear in our oral data.

**Patients and methods.** A written and an oral argumentation produced by 25 participants between 9 and 11 years of age were analysed. In the written task, the children wrote their argumentations, and in the oral task their argumentative interaction with a collaborator was videotaped and later the types of arguments used in each case (logical, fallacies, sanctioning or moralist) were analysed.

**Results**. There is an obvious difference between the results in the two tests, which suggests the need to review the verbal evaluation mechanisms and to complete the written results with oral skill tests. The problems normally associated with written tasks do not appear in oral language; participants are able to follow the discursive thread and to provide new arguments related with the topic.

**Conclusions**. The data obtained highlight the added difficulty of a written task for children with ADHD, the reliability of the oral results with regard to linguistic skills, and the need to use both types of data in evaluations.

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## Rev Neurol. 2014;58:S43-S49.

# PHARMACOLOGICAL MANAGEMENT OF ATTENTION DEFICIT HYPERACTIVITY DISORDER WITH METHYLPHENIDATE AND ATOMOXETINE WITHIN A CONTEXT OF EPILEPSY.

## Mulas F, Roca P, Ros-Cervera G, et al.

**Introduction**. The prevalence of attention deficit hyperactivity disorder (ADHD) in patients with epilepsy stands at around 30-40%, especially the inattentive subtype, while other studies on children diagnosed with ADHD show figures that vary from 6.1% to 30% which present alterations in the electroencephalogram and epilepsy problems. Although clinical practice guidelines advise against treatment with psychostimulants in ADHD that is comorbid with epilepsy, especially when the latter is not considered active, some researchers and practitioners recommend caution as regards beginning this pharmacological therapy, while less research has been conducted on the use of non-psychostimulants.

**Aim**. To review the patient records of children with epilepsy and ADHD who received pharmacological treatment with psychostimulants and non-psychostimulants for an attention disorder. Patients and methods. The study involved a sample of 23 patients aged 5-16 years. The type of epilepsy and the clinical course and electroencephalogram were analysed at both one and two years after beginning pharmacological treatment of ADHD.

**Results**. At two years, one patient presented a crisis and two patients continued to display paroxysmal activity in the electroencephalogram.

**Conclusions.** The data presented show that pharmacological treatment of ADHD does not exacerbate the epilepsy in well-controlled patients, although it is advisable to take into account factors such as the type of antiepileptic drug, the type of drug for ADHD and the cognitive profile, in order to favour a satisfactory development. In epileptic children with learning difficulties, it is

## **NEWSLETTER – ADHD**

necessary to evaluate the mechanisms involved in attentional processes, since they may well be compromised and in need of a more specific treatment.

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## Rev Neurol. 2014;58:S71-S75.

DEPRESSIVE PHENOMENOLOGY AT THE OUTSET OF NEUROPAEDIATRIC DISEASES. *Narbona J.* 

**Introduction**. Depressive phenomenology, in its diverse nosological forms, affects 8-10% of children and adolescents of general population. Most frequently mood disorders have a primary origin, following poligenic multifactorial model. Moreover there is a non negligible proportion of cases in which depressive symptoms accompany neurological illnesses or they even constitute a part of predominant manifestations at the clinical start of neurologic disease, or mark a point of inflexion in its course.

The aim of the present article is to review relevant literature dealing with this topic.

**Development**. A significative higher frequency of depressive phenomenology, not explainable by hazard, can be an early manifestation in children and adolescents with: epileptic syndromes, sleep disorders, chronic recurrent cephalalgias, several neurometabolic diseases, and intracranial tumors. Points of coincidence have been shown in dysequilibrium of brain neurotransmitters (serotonine, noradrenaline, hyperglutamatergic states) which could not be hypothesized as maintaining both neurological and mood conditions.

**Conclusions**. The suspiction of a neurological disease should be adopted in cases of mood disorder not easily explainable by familial antecedents or clear biographical stressors. The search for a brain disorder by means of a meticulous anamnesis and neurological clinical and ancillary exams makes possible to discover the brain disorder at a very early stage and ameliorate the chances of accurately manage both the neurological and mood disorders. The simultaneous treatment of both dimension of the illness helps to improve the patients' quality of life.

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Rev Neurol. 2014;58:S31-S36.

DISCIPLINE STYLES AND CO-MORBID DISORDERS OF ADOLESCENTS WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER: A LONGITUDINAL STUDY.

## Colomer-Diago C, Berenguer-Forner C, Tarraga-Minguez R, et al.

**Introduction**. Problems in cognitive functioning, social and educational development of children with attention deficit hyperactivity disorder (ADHD) continue to be present in adolescence and adulthood. Although the literature shows a significant relationship between the use of dysfunctional discipline methods and severity in the course of ADHD, follow-up studies have been rare.

**Aims**. To analyze parenting style and ADHD symptomatology assessed in childhood (time 1) to predict the oppositional behavior and cognitive problems in early adolescence (time 2), and to study, depending on the use of dysfunctional parenting style, the course of oppositional behavior and cognitive problems.

**Patients and methods**. Forty-five children with ADHD-combined presentation were assessed in two different moments: time 1 (ages: 6-13) and time 2 (ages: 8-16).

**Results**. Oppositionism and cognitive problems in the follow-up were predicted by dysfunctional discipline styles and ADHD severity (assessed in time 1). Oppositional behavior increased between time 1 and time 2 in children with a dysfunctional parenting, whereas a decrease on

oppositional symptoms was observed in the functional parenting group (time null discipline interaction effect).

**Conclusions**. Dysfunctional parenting practices in childhood predicted cognitive and behavioral problems associated in adolescence. The findings have implications for the planning of interventions.

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### Rev Neurol. 2014;58:S25-S30.

## PASSIVE TACTILE STIMULATION AND ITS CLINICAL AND NEUROPHYSIOLOGICAL REPERCUSSIONS (P300) IN BLIND CHILDREN WITH SYMPTOMS OF ATTENTION DEFICIT DISORDER.

## Serrano-Marugan I, Herrera B, Romero S, et al.

**Introduction**. Tactile stimulation is key for the posterior brain re-organization activity and attention processes, however the impact of tactile stimulation on attention deficit disorder (ADD) in blind children remains unexplored.

**Subjects and methods**. We carried out a study with children having or not ADD (four per group). The subjects have been exposed during six months to tactile stimulation protocol consisting in two daily sessions (morning and afternoon sessions) of 30 minutes each. We have measured the ability to detect an infrequent tactile stimulus, reaction time, latency of P300, sources of brain activity, and ADD clinical symptoms, before and after tactile training.

**Results**. Passive tactile stimulation significantly improves ADD clinical symptoms, particularly attention, behavior and self-control of involuntary movements and tics. In addition, tactile stimulation changes the pattern of brain activity in ADD blind children inducing activity in frontal and occipital areas, which could be associated to a compensation of the attention deficit.

**Conclusion**. Passive tactile stimulation training may improve ADD clinical symptoms and can reorganize the pattern of brain activity in blind ADD children.

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## Rev Neurol. 2014;58:S51-S56.

## THE **P300** COMPONENT AS A NEUROPHYSIOLOGICAL CORRELATE OF BEHAVIOURAL WORKING MEMORY IN ADOLESCENTS WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER.

## Roca P, Presentacion-Herrero MJ, Miranda-Casas A, et al.

**Introduction**. Deficit in the executive functions has been widely studied in attention deficit hyperactivity disorder (ADHD). The interest in its neurophysiological correlates has led to an improvement in the identification of the symptoms, the characteristics and the treatment of the disor der.

**Aims**. The objective of this study was to analyse the correlation between latency and amplitude of the P300 component and an ecological measure of working memory in a sample of adolescents. Patients and methods. The sample consisted of 24 boys and 7 girls aged between 12 and 18 years. P300 cognitive evoked potentials in auditory mode at Cz were registered and analysed. Furthermore, the parents filled in an executive behaviour home rating scale (BRIEF), which the working memory index was extracted from.

**Results**. Significant correlations were found between the P300 amplitude and the working memory index of the BRIEF-P.

**Conclusions**. Results underline the usefulness of the P300 component for the study of its executive correlates, as well as the need to conduct further studies involving larger samples and greater complexity.

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#### Rev Neurol. 2014;58:S3-S18.

BRAIN ABNORMALITIES IN ATTENTION-DEFICIT HYPERACTIVITY DISORDER: A REVIEW. *Rubia K, Alegria AA, Brinson H.* 

**Aim**. To review the magnetic resonance imaging findings in child and adult attention-deficit hyperactivity disorder (ADHD).

**Development.** Studies have shown that ADHD is characterised by multiple functional and structural neural network abnormalities including most prominently fronto-striatal, but also fronto-parieto-temporal, fronto-cerebellar and even fronto-limbic networks. Evidence from longitudinal structural imaging studies has shown that ADHD is characterised by a delay in structural brain maturation. This is reinforced by indirect evidence from cross-sectional imaging studies for more immature brain function as well as structural and functional connectivity patterns, which, however, needs corroboration by longitudinal studies. Dysfunction of the ventrolateral prefrontal cortex seems to be more pronounced in ADHD relative to other pediatric disorders and there is some evidence for differential abnormalities in the basal ganglia. A meta-analysis of stimulant effects on brain function shows that the most consistent mechanism of action of acute psychostimulant medication is the increased activation of the inferior prefrontal cortex and the basal ganglia. First attempts to use neuroimaging data to make individual diagnostic classifications of ADHD children based on pattern recognition techniques are promising but need replication across centres and scanners.

**Conclusions**. The last two decades of neuroimaging have shaped out biomarkers of ADHD. Future studies will need to focus on using this information for clinical translation such as using neuroimaging for individual diagnostic and prognostic classification or by using neuroimaging as a neurotherapy to reverse those brain function abnormalities that have been established over the last two decades of neuroimaging.

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#### Riv Psichiatr. 2013;48:448-55.

**ADHD** SYMPTOMS AS RISK FACTORS FOR DYSFUNCTIONAL EATING HABITS IN ADOLESCENTS: RESULTS FROM A LONGITUDINAL STUDY.

## Petrone P, Prunas A, Dazzi S, et al.

**Aim**. The aim of this study is to analyze the relationship between attention deficit hyperactivity disorder (ADHD) symptoms in childhood and early-adolescence and the development of dysfunctional eating habits later in life. The sample under investigation is composed of 217 adolescents (males: 30.9%; mean age: 17.1 (plus or minus) 0.88 ys; range: 16-19 ys) voluntarily recruited in the city of Parma (Northern Italy) in the context of a longitudinal research project focused on developmental factors of antisocial behaviour. All subjects were assessed at T1 (mean age: 12 ys) and at T2 (mean age: 14 ys) using a structured clinical interview to collect information on ADHD symptoms on a lifetime basis and, at T3 (mean age: 17 ys), they were administered an interview to assess pathological eating habits. Correlation and regression analyses were carried out between scores of the three symptom domains of ADHD and eating habits as assessed at T3.

**Results** suggest that the association between ADHD symptoms and eating habits show differences according to gender, in that in females ADHD symptoms assessed at T2 are associated with compensatory behaviours, while in males they are predictive of overweight as assessed at T3. ADHD symptoms, although under threshold, may lead to chaotic and unorganized eating habits which might put female at risk for compensatory behaviours and males for overweight.

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### P.3.024 Face and emotion recognition in children with ADHD and autism spectrum disorders: Effects of methylphenidate

F. Placini<sup>1</sup>\*, C. Peddis<sup>1</sup>, S. Carucci<sup>1</sup>, S. Petza<sup>1</sup>, C. Balia<sup>1</sup>, J.A. Sergeant<sup>2</sup>, A. Zuddas<sup>1</sup>. <sup>1</sup>University of Cagliari, Biomedical Science Centre for Pharmacological Therapies in Child & Adolescent Neuropsychiatry, Cagliari, Italy; <sup>2</sup>Vrije Universiteit, Clinical Neuropsychology, Amsterdam, The Netherlands

**Objective:** The object of this study was to compare Autism Spectrum Disorders (ASD), Attention Deficit Hyperactivity Disorder (ADHD) and Typically Developing Children (TDC) while processing facial emotions and Clinical neuropsychopharmacology

matching emotions by using the Amsterdam Neuropsychological Test battery (ANT). We also examined the influence of treatment with methylphenidate in ADHD patients performing the same ANT tasks.

Patterns and timing of recognition of emotional facial expression are potential markers of cognitive dysfunction in both ADHD and ASD: reaction time (RT) studies provide ample evidence that processing speed is a sensitive parameter in the experimental and clinical evaluation of neuropsychological functions [1,2]. Few studies, however, have been designed to compare these patterns in both ASD and ADHD children using the same neuropsychological tasks.

Methods: Facial Recognition (FR), Identification Facial Emotion (IFE) and Matching Facial Emotion (MFE) were assessed in 35 drug-free ADHD, 31 ASD and 36 TDC aged 6 to 14 and IQ>70 by reaction time (RT) correct (RTC), RT to errors (RTE) and Errors. FR consists of processing neutral faces; IFE includes eight emotions: happy, sad, angry, fear (four basic emotions), disgust, surprise, shame, and contempt (four complex emotions); MFE task includes four basic emotions. Data about performance in the same tasks for a subgroup of ADHD patients before and during MPH treatment have also been collected.

Statistical analyses were performed using SPSS. A multifactorial analysis of variance (MANOVA) was used for comparisons between sets of data in order to examine group differences. Pearson correlations were carried out between the different emotion variables and the IQ, age, C-GAS and CGI.

**Results:** We examined the effect of the three contrasting tasks with respect to Emotional processing using three dependent variables: Reaction Time of correct answers (RTc), RT of errors (RTe) and errors. ADHD children were significantly slower and less accurate than TDCs in both FR and IFE tasks. A significant main effect for group, task and a significant interaction between task and group were found for the FR versus IFE task for both RT and number of errors. Both the ASD and ADHD groups compared with the TDC group were slower; difference in RT between IFE and FR tasks was significant in the ADHD compared with TDC group. Findings could not be explained by a speed-accuracy trade-off difference between groups or by IQ.

Analyses about the effect of methylphenidate in a subgroup of ADHD patients are in due course and will be presented during the poster session.

**Conclusions:** The results suggest that specific information processing deficits are present in both ADHD and ASD participants compared to TDC (slower reaction time and larger error rates) especially during face recognition and identification of facial emotions stimuli, having specific differences in processing facial emotions. Methylphenidate possibly exerts a significant effect on the performance of ADHD children.

In clinical population such as for ADHD and ASD children, specific neuropsychological tasks should be administered to better characterize specific strengths and difficulties in their cognitive functioning and, in turn, to develop efficient treatment strategies for improving social abilities.

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#### P.3.025 The acute stress response in euthymic bipolar disorder patients and their siblings

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Introduction: Exposure to chronic or excessive stress is associated with the development of manic and depressive episodes in bipolar 1 disorder (BD1). Additionally, early life trauma negatively influences the clinical course and outcome of bipolar disorder with an earlier onset, a rapid cycling course, increased psychotic symptoms, and suicidal behavior [1]. Despite the important role of stress in BD1, our current understanding of stress system functionality in BD1 is limited. It is known that basal functionality of the endocrine and sympathetic system in BD1 patients is altered with an increased cortisol awakening response [2] and an increased sympathetic nervous system (SNS) tone [3]. These changes could reflect an insufficiently buffered stress system with, as a result, an impaired capacity to adapt to stress. Increased insight into the dynamics of the endocrine and sympathetic stress response in BD1 patients may increase our understanding of the vulnerability for stressful challenges in bipolar disorder. Moreover, it is unknown whether altered stress reactivity in BD1 is the result of BD1 itself or whether an increased genetic vulnerability for BD1 independent of disease status plays a role. Such an increased genetic risk for BD1 is present in siblings of BD1 patients. If a genetic BD1 predisposition would

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## Pediatric Reports 2013; volume 5:e18

## Early precursors of low attention and hyperactivity in moderately and very preterm children at preschool age

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#### Abstract

The low attention and hyperactivity are major morbidities associated with very and moderately preterm birth. The study has been aimed at investigating the likely occurrence of early precursors of Attention Deficit and Hyperactivity Disorder (ADHD) in very and moderately preterm children at preschool age. The involved children were: 25 very preterm children (M=29.4 weeks of gestational age, SD=2), with low birth weight (M=1200 g, SD=250 g); 35 moderately preterm children (M=34.6 weeks of gestational age, SD=1) with low birth weight (M=2100 g, SD=250 g); 60 healthy full-term children as the control group. Parents of children have been administered specific questionnaires to detect low attention and hyperactivity of their children at home. The data have shown the risk of precursors of ADHD, highlighting statistically significant birth-related differences in both hyperactivity/impulsivity [F(2,119)=3.5, P=0.03, η<sup>2</sup>=0.06] and inattention [F<sub>(2,119)</sub>=2.4, P=0.04,  $\eta^2=0.04$ ], where very preterm children have got higher scores in these two dimensions compared with full-term and moderately preterm children. The very preterm children have got higher scores of impulsivity and inattention than the full-term children (Tukey'HSD - Honestly Significant Difference; P<0.001).

### Introduction

Preterm birth, either severe (gestational age <28 weeks or low birth weight <1500 g) or moderate (gestational age <34/5 weeks and weight <2500/>500 g), is a risk condition at cognitive, behavioral and socio-relational levels.<sup>14</sup>.

The interruption of the fetal maturation, even when occurs at  $32^{nd}$  or  $36^{th}$  of the gestational week, leads to cerebral immaturity at birth,<sup>5-7</sup> a risk for the cognitive development of preterm children,<sup>8-10</sup> as well as attention deficit and hyperactivity disorder (ADHD).11-15

Studies on medium and long-term outcomes have shown that 50-70% of very low birthweight (VLBW) infants, even in the absence of major disabilities, would display learning difficulties, attention-deficit/hyperactivity disorder, specific neuropsychological deficits, and behavioral problems.<sup>11-14</sup> It has been established that VLBW infants are more likely to develop visual perceptual and visual-motor impairments; delay in some of the language functions and working memory deficit. They may also have learning problems and attention deficit at school age.<sup>10,16</sup>

Other studies of the field also have suggested that moderately preterm children (GA >32/<35 weeks) show attention and self-control disorders since preschool age, though at a less severe level when compared with severely preterm cases.1.6-7.16

As an extension of such research projects, this study has been aimed at identifying the presence of early precursors of low attention and hyperactivity (ADHD) in late and very preterm children at preschool age,<sup>17</sup> characterized by distraction, impulsiveness and hyperactivity within their family environment (home). Therefore, taking in consideration the possible differences due to the gender, it has been verified the presence of statistically significant differences between moderately preterm, very preterm and full-term children at preschool age, with relation to the precursors of ADHD (low attention/distraction, hyperactivity/impulsivity).

The study has provided an innovative contribution with respect to the literature of the field, because it has mainly focused on the precursors of ADHD rather than on its symptoms; it has investigated the precursors of ADHD at preschool rather than at school age. However, the study is an extension of those studies focused on very and moderately preterm children, 6.7.18 even though they deal with groups of preterm children at school age or adult age.

The study has investigated specific indicators of the precursors of ADHD, identified as inattention meant as distraction during recreational activities and in following instructions to fulfill an activity. A wide literature has shown that preterm children are less capable to focus attention on objects or activities,<sup>9,19,20</sup> as well as to activate cognitive processes (gathering and selecting information, concentration...) functional for a more rational adjustment to situations.<sup>21,22</sup>

Among these indicators, hyperactivity includes restlessness; difficulties in *calm* play activities; motor activity modulation disorder with consequential clumsy and uncoordinated movements with a reckless motor behavior.<sup>17</sup> Motor development impairments occur in very preterm children especially with regard to the capacity of modulation of fine motor skills and

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Key words: precursors, inattention, hyperactivity, preterm children, preschool age.

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Contributions: MRM, GP, CP, conceived and designed the research project, acquired, analyzed and interpreted the data, wrote the relevant article and critically revised it; GS, interpreted the data and results and shared some reflections concerning the article; CM, administered the instruments to parents and checked their results.

Conflict of interests: the authors declare no potential conflict of interests.

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visuospatial coordination.<sup>23,24</sup> Impulsivity is another indicator linked to hyperactivity. It is displayed as behavioral, self-regulation motor skills and self-control impairments. Due to impulsivity, the child has difficulty in respecting the roles, waiting for his/her turn-taking, modulating his/her relationship with the other, intervening in and *invading* others' activities (plays, conversations, etc.) and s/he is not able to stay still in long waits or postponing gratifications.<sup>25</sup>

### Materials and Methods

#### Participants

The research group (Table 1), has been made up of 120 children at the average age of 5 years and 2 months. The children have been selected within some of the local schools and the Neonatal Intensive Care Unit (NICU) of





the Hospital of Palermo, Italy

The children collected in the NICU have been very preterm and they were still undergoing the follow-up monitoring of the development trend up to school age, performed by the hospital service. All the children involved have been healthy preterm (*i.e.* without any neurologic impairments due to crebral hemorrhage at neonatal phase, nor organic alterations), even though they have been at high risk (GA <30 weeks and birth weight <1500 g).

The moderately preterm, as well as the fullterm children (*i.e.* the control group) have been collected in the local schools. They have been chosen by means of a survey on birth carried out in the classroom. The parents of children have been asked to answer some simple questions about the birth of their children (*my* son was born on...; my son was born in...; my son was born prematurely...; the birth weight of my son was...; my son was hospitalized for...). These information have been compared with those of the discharge report provided by the Neonatology Unit.

Before involving the research group children, the official authorities had approved the proposed path in terms of correctness and ethics. Then the children's parents have been asked to sign the declaration of informed consent according to the Italian Legislative Decree 196/2003 art.13 related to their personal and other people's data protection. Professionals working in the field have followed the official path respecting the criteria that regulate the main codes of ethics of the study, according to a wide research project of the Unit of Research in Pediatric Psychology conducted by the Psychology Department of the University of Palermo.

The involved children have been divided

into three groups comparable for socio-cultural features: 25 very preterm children (M=29.4 weeks of gestational age, SD=2), with low birth weight (M=1200 g, SD=250 g), selected according to the following criteria: gestational age <32 weeks, birth weight 1500 to 2500 g, lack of neurologic pathology; sensorial deficit and genetic pathology or malformative syndrome. It has been a small group of preterm children at low risk for adverse cognitive sequelae and it has not displayed any neurological problem during their hospitalization.

Thirty-five moderately preterm children (M=34.6 weeks of gestational age, SD=1) without any medical neonatal and/or complications and low birth weight (M=2100 g, SD=250 g), selected according to the following criteria: gestational age <35 weeks, birth weight 1500 to 2500 g without any neurologic pathology, sensorial and genetic pathology deficit, nor malformative syndrome.

Sixty healthy full-term children (M=40 weeks gestational age without any pre- and perinatal complications). The selection criteria of the control group have been: about 40<sup>th</sup> post-conceptional week at birth (range=39-41 gestational weeks); birth weight >2500 g; lack of pre- and perinatal complications, and lack of neurologic pathology, sensorial deficit and genetic pathology or malformative syndrome.

In relation to the family's socioeconomic status and the socio-family background of the research group (Table 1), the children of the three groups have not differed in a significant way. The groups that have been compared seem to overlap, as shown in certain statistical tests (test t,  $\chi^2$ ).

The full term and preterm children belonged to Italian families; 90% of them have siblings (two children per family on average), whose mother (32 years old on average) belonged to a social middle class (one-income family), with secondary school education on average.

#### Procedures and instruments

It has been used a questionnaire to observe the behavior of children at home, the IPDDAG Italian Scale (Attention Deficit Hyperactivity Disorder Early Detection for Parents).<sup>26,27</sup> It is a specific questionnaire aimed to the detection of children defined at risk of ADHD during preschool age, performed through the assessment of parents.

In particular, the questionnaire has been administered to the parents of the children. They have been asked to evaluate through a 4response Likert-type scale (0= not at all/never; 1= rarely/sometimes; 2=quite frequently/most of the time; very frequently/always) how frequently they had observed a particular behavior their children displayed at home.

The questionnaire is made up of 14 items expressed in a negative form, whose odd items refer to inattention, related to the difficulty the child has in prolonging his/her attention on an activity and plays at home, while the even items refer to *impulsivity/hyperactivity* meant as motor restlessness and self-control and selfregulation disorders. Five more final items have also been to be considered related to risk factors (*i.e.* forms of socio-cultural disadvantage, poor cognitive potentialities, presence of emotional and/or relational impairments and likely family troubles).

The instrument has been designed by Re and Cornoldi, according to the Italian normative sample;<sup>26,27</sup> the content of items refers to other previous questionnaires – addressed to parents in order to assess inattention and hyperactivity behavior of children at school

#### Table 1. Prenatal and family characteristics of the sample by term and preterm birth.

| Variable                          | Very | pretern                    | 1 (=25)*    | Mode          | rately pret                    | erm (=35) | Full | -term                | (=60)*    | P value |
|-----------------------------------|------|----------------------------|-------------|---------------|--------------------------------|-----------|------|----------------------|-----------|---------|
|                                   | Mean |                            | Range       | Mean          |                                | Range     | Mean |                      |           |         |
|                                   |      |                            | Clini       | cal character | ristics                        |           |      |                      |           |         |
| Gender                            |      | nale: 15 (6<br>ale: 10 (40 |             |               | male: 15 (439<br>lale: 20 (57% |           |      | ale: 35<br>le: 25 (4 |           |         |
| Child age (months)                | 62   | 3                          | 57-67       | 62            | 4                              | 57-67     | 64   | 2.5                  | 61-66     | n.s.    |
| Birth gestational age             | 29.4 | 2                          | 26-31       | 34.6          | 1                              | 33-35     | 40   | 2                    | 38-42     | <0.05   |
| Birth weight (g)                  | 1200 | 250                        | 950-1450    | 2100          | 250                            | 1950-2350 | 3200 | 300                  | 2900-3500 | < 0.05  |
| Days of hospitalization           | 80   | 10                         | 70-90       | 15            | 8                              | 8-23      | 2    | 1.5                  | 2-3       | < 0.05  |
|                                   |      |                            | Family's ba | ckground ch   | aracteristi                    | CS        |      |                      |           |         |
| Household income                  | 1    | 1                          | 1-2         | 1             | 1                              | 1-2       | 1    | 1                    | 1-2       | n.s.    |
| Number of working parents         | 1    | 1                          | 1-2         | 1             | 1                              | 1-2       | 1    | 1                    | 1-2       | n.s.    |
| Education level of mother (years) | 13   | 8                          | 8-23        | 12            | 8                              | 8-22      | 12   | 8                    | 8-22      | n.s.    |
| Mother's age (years)              | 31.6 | 6                          | 24-37       | 32.6          | 5                              | 26-38     | 29.6 | 5                    | 24-34     | n.s.    |
| Number of children                | 2    | 1.5                        | 1-3         | 2             | 1.5                            | 1-4       | 2    | 1.5                  | 1-4       | n.s.    |

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age, DSM-IV criteria and Kendall and Wilcox's Scale. The validity of the scale has been verified through a factorial analysis whose results show that the division of items in components (inattention and hyperactivity) have been realized. The values of Pearson's coefficients of correlation and Cronbach's alpha value have shown a good internal coherence of the instrument. The predictive quality of the instrument has been very good.

The higher the score, the larger the presence of patognomonic tracts of the disorder has been.

This questionnaire allows to detect children at risk of attention difficulties and hyperactivity on the basis of the score in the sub-scale; with regard to reading and interpreting the result, a score equal to or more than 14 (cut-off score) shows the presence of a likely risk of ADHD at preschool age (*impulsivity/hyperactivity scale*: mean score = 13.70, SD=4.30; *inattention scale*: mean score = 11.70, SD=3.80).

#### Results

Data treatment and analysis

The statistic program for Social Sciences -SPSS 16 has been used to analyze the data.

The Kolmogorov-Smirnov's test has been used to verify the presence of a normal distribution of the scores obtained for each of the two scales of the IPDDAG (P>0.05) and the Levene's test has been used to verify the equality of variances in the three samples (homogeneity of variance) (P>0.05). Then, a multivaried covariance (MANCOVA) with continuous variables (scores related to the two scales) 3 (birth) X2 (gender) has been used, and birth weight has been analyzed as the covariate variable. The likely differences between the scores of the two scales (dependent variables) have been analyzed considering birth (Term/Very and Moderately Preterm) and gender (F/M) as independent variables, and the birth weight as covariate variable. A value of P<0.05 has been considered significant.

A post-hoc test (Tukey'HSD – Honestly Significant Difference) has been used in order to determine which groups (full term, late preterm and very preterm children) has differed from each other. The  $\chi^2$  test has been used to calculate the significance of the number of children (frequencies) of each group, who has exceeded the cut-off score of the instrument (number of children with lower than, equal to or higher than the cut-off).

The results of the multivariate analysis have only showed significant effects of the birth (Wilks'  $\lambda$ =0.93,  $F_{(4,119)}$ =1.81, P=0.048,  $\eta^2$ =0.32).

There have not been statistically significant effects related to the variables birth weight (Wilks'  $\lambda$ =0.99,  $F_{(2,119)}$ =0.032, P=0.13,  $\eta^2$ =0.001), gender (Wilks'  $\lambda$ =0.91,  $F_{(2,119)}$ =5.11, P=0.13,  $\eta^2$ =0.032) and birth X gender (Wilks'  $\lambda$ =0.96,  $F_{(4,119)}$ =1.08, P=0.36,  $\eta^2$ =0.02). The children of the research group have got indifferently high scores of inattention and hyperactivity, whatever their gender and birth weight has been. The period of gestation, conversely, has seemed to be the sole variable that has significantly affected the attention and hyperactivity field.

The preterm and full-term children have differed with relation to the presence of low attention and hyperactivity/impulsivity; the parents have shown statistically significant differences related to preterm birth in both hyperactivity/impulsivity [ $F_{(2,119)}=3.5$ , P=0.03,  $\eta^2=0.06$ ] and inattention [ $F_{(2,119)}=2.4$ , P=0.04,  $\eta^2=0.04$ ], where the very preterm children have got higher scores in these two dimensions compared to the full-term and late preterm children (Table 2). The parents have reported a description of preterm children'



behavior as children who, regardless of their gender, not only had shown attention deficit at home, but they had also shown restlessness, excessive movements, difficulties in modulating motor skills activities with clumsy uncoordinated reckless and not aimed movements.

The children's scores also have differed depending on preterm or full-term birth: the very and moderately preterm children at preschool age have shown higher scores of *impul-sivity* than full-term children (Tukey'HSD P<0.001); the very and moderately preterm children have also shown higher scores of *inattention* than full-term children (Tukey'HSD P<0.001). The very and moderately preterm children have not differed in relation to *impulsivity* and *inattention* (Table 3).

In relation to such data, from a solely descriptive point of view, it has to be considered the relevance of the frequencies of preterm children with regard to the scores of hyperactivity and inattention precursors since they are close to the cut off score fixed in the questionnaire. 20% of the moderately preterm children (no. 7) and 20% of the very preterm children (no. 5) exceed the cut-off score being at risk of *inattention*, and 20% of the full term children (no. 6) would seem to be at risk and 5% of them is on the edge (no. 3). A large number of children with low attention ( $\chi^2$ =6.6, gf=2, P=0.03) have been identified.

With regards to *hyperactivity/impulsivity*, 20% of the moderately preterm children (no. 7) and 40% of the very preterm children (no. 10) would seem to be at risk and 20% is on the edge (no. 57); 20% of the full-term children are at risk (no. 12) and 5% of them are on the edge (no. 3). Even in this case, the number of preterm children displaying precursors of hyperactivity, appears statistically higher compared to the group of full-term children ( $\chi^2$ =17.7, gf=2, P=0.001).

#### Table 2. Precursors of attention deficit and hyperactivity/impulsivity in research group.

|                  |              | Very<br>preterm<br>children |                      |              | loderately<br>preterm<br>children |                      |              | Term<br>children       |                      | Tests (  | of between<br>effects                                   | subjects  |
|------------------|--------------|-----------------------------|----------------------|--------------|-----------------------------------|----------------------|--------------|------------------------|----------------------|--|---|---|
| Scales<br>IPDDAG | Mean<br>(SD) | Mean<br>female<br>(SD)      | Mean<br>male<br>(SD) | Mean<br>(SD) | Mean<br>female<br>(SD)            | Mean<br>male<br>(SD) | Mean<br>(SD) | Mean<br>female<br>(SD) | Mean<br>male<br>(SD) | Birth<br>(VP/MPT/T)  | Gender<br>(M/F)   | Gender<br>birth   |
| Inat             | 9.2 (7.5)    | 10.1 (9)                    | 7.1 (4.1)            | 8.9 (4.9)    | 8.8 (5.7)                         | 8.9 (4.4)            | 5.4 (4)      | 6 (4.6)                | 4.4 (2.3)            | F (2,119) 2.4<br>sign. <0.05<br>η <sup>2</sup> 0.04            | $\frac{F_{(1,119)}}{n.s.} \frac{2.5}{\eta^2 \ 0.02}$    | F <sub>(2,119)</sub> .9<br>n.s.<br>η <sup>2</sup> 0.02  |
| Hyp/Imp          | 12.5 (7.4)   | 12.3 (7.8)                  | 12.8 (7)             | 11.9 (4.6)   | 10.6 (4.2)                        | 13.2 (4.3)           | 8 (2.5)      | 7.9 (2.6)              | 8.1 (2.4)            | F <sub>(2,119)</sub> 3.5<br>sign. <0.05<br>η <sup>2</sup> 0.06 | F <sub>(1,119)</sub> 1.4<br>n.s.<br>η <sup>2</sup> 0.01 | F <sub>(2,119)</sub> 1.8<br>n.s.<br>η <sup>2</sup> 0.03 |

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## **Discussion and Conclusions**

The purpose of this study has been to explore the relation between preterm birth and the outcome at age 5 in preterm children at low risk of adverse *squelae*. As it has been hypothesized, and like other studies have shown,<sup>28,30</sup> low attention and hyperactivity have been displayed by preterm children at preschool age.

The main results of the study have shown the presence of a profile of preterm children who, even at preschool age, are *at risk* of precursors of attention deficit and hyperactivity disorder. The preterm children of the present experimental group, especially the very preterm, have been reported as being hyperactive and restless children at home, showing difficulties in self-regulating and self-controlling during calm play activities.

The relevance of some data of the research lies on the lack of significant effects linked to gender and birth-weight, unlikely other contributions of the field.<sup>20-31</sup> It would seem that being male or female is not a risk factor of attention disorder and hyperactivity for the children involved in the research, even though male children have shown higher tendency to be more hyperactive and distracted than female, as it has been also reported by a wide literature of the field and early studies.<sup>31</sup>

These conclusions must be tempered by the fact that the children have been evaluated for ADHD symptoms, not for a clinical diagnosis of ADHD. Although prematurity, perinatal morbidity, and toddlerhood neurological and medical health status predict these symptoms at age 4, additional work is needed to make these connections to the clinical diagnosis of ADHD at a later age.

The different percentage of the children who are at risk of precursors of ADHD at preschool age, for having exceeded the cut-off score of the instrument, is another important outcome. The neonatal clinic history of the children involved has not been characterized by any cerebral hemorrhage, nor by neurologic *sequelae*. During their hospitalization at the NICU not any severe hypoglycaemic shock occurred, nor long periods of supplemental oxygenation (intubation) were necessary. That underlines the individual valence of the developmental path of each child and of the reference family environment that, although it has been little detected by the analyses performed by this study, has not been characterized by any psychosocial risk factors (*i.e.* smoking during pregnancy; use/abuse of substances; risk factors due to psychiatric or relational pathologies, etc.).<sup>32-34</sup>

Such data trace a similarity between the maturative and developmental path of the severely preterm children (<32 weeks) and that of the moderately preterm highlighting,<sup>6</sup> even in the latter case, likely risks linked to moderately preterm birth. Such data comply with those studies that have shown that severe and moderate prematurity is a factor that may affect the development of impulsivity regulation,<sup>6,11</sup> self-regulation and behavior and motor self-control processes (as well as concentration and attention skills).

The levels of maturity of the physiological brain processes of fetus reached before their interruption caused by birth at 34 weeks are important too,<sup>6</sup> because together with the genetic and environmental factors (*i.e.* early interaction with hospital environment, medical treatments, relationships with parents, external stimuli, etc.), contribute to trace problems and slight disorders only occurring in terms of *slowness* and/or difficulty at preschool and school age.

These data establish an initial level of behavior in the children of the research group, which can potentially lead to precursors of school-age deficit and/or hyperactivity disorder. By comparing the data of the follow-up after two years, it is possible to check the stability or the change in trend. **Clinical implications** 

Due to the increasing survival rate of preterm infants, the impact of perinatal morbidities and their relationship to low attention and hyperactivity pose an important developmental question: are the preterm children with high neonatal risk who display low attention and high activity at age 5, at an increased risk of developing ADHD?

Further longitudinal studies are needed using diagnostic measures to answer this question.

However, the results should not make the moderately preterm child's development pathological, nor make it always requiring medicalization.

The study suggests the need of hypothesizing, not only in the case of severe prematurity, specific paths of assessment of the various evolutional dimensions of children aimed at monitoring certain aspects of their cognitive, motor, socio-relational and behavioral development. The assessment and screening up to school age are aimed at an early identification of problematic areas of attention and self-regulation.

The study claims the need to activate a follow-up of the preterm children and a developmental monitoring, performed by pediatricians through developmental scales such as the Griffith's Mental Development Scales.<sup>35</sup>

The study also provides some hints for prevention of ADHD risk in preterm children. Early training courses should be addressed to preschool children to help them develop selfregulation skills (*i.e.* emotional, cognitive, relational and behavioral). Such courses should also be addressed to parents in order to help them develop their parental competencies, useful for facing behavioral problems related to everyday life.

#### Limits of the study

Some final considerations about the limits of this study have to be made. One of the lim-

| Variable                  | Birth (1)                             | Birth (J)          | Differences between means (1-J) | Std. error | P value |
|---------------------------|---------------------------------------|--------------------|---------------------------------|------------|---------|
| Hyperactivity/impulsivity | Full term                             | Moderately preterm | -4.17                           | 1.09       | 0.001   |
| 800 (C. C. C. C.          |                                       | Very preterm       | -4.65                           | 0.98       | 0.001   |
|                           | Moderately preterm                    | Full term          | 4.17                            | 1.09       | 0.001   |
|                           |                                       | Very preterm       | -0.48                           | 1.19       | n.s.    |
|                           | Very preterm                          | Full term          | 4.65                            | 0.98       | 0.001   |
|                           |                                       | Moderately preterm | 0.48                            | 1.19       | n.s.    |
| Inattention               | Full term                             | Moderately preterm | -3.83                           | 1.24       | 0.007   |
|                           |                                       | Very preterm       | -3.54                           | 1.11       | 0.005   |
|                           | Moderately preterm                    | Full term          | 3.83                            | 1.24       | 0.007   |
|                           |                                       | Very preterm       | 0.28                            | 1.35       | n.s.    |
|                           | Very preterm                          | Full term          | 3.54                            | 1.11       | 0.005   |
|                           | 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 | Moderately preterm | -0.28                           | 1.35       | n.s.    |

Table 3. Differences between groups for birth (full term, moderately preterm, very preterm): Tukey's HSD Test (Honestly Significant Difference).

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its can be the little number of participants, drawing conclusions that cannot be generalized, highlighting possible affections of the development of the moderately and very preterm children. Furthermore, the composition of the sample size of this research project does not include children with important cognitive sequelae, enhancing the chance of spurious findings, or minimally that the magnitude of the observed relations will not be as high when a larger sample is studied. These considerations suggest the importance of other studies on preterm infants who had cerebral palsy to better understand their develop mental trend. This is the only way to explore the predictive value of the different variables.

Another limit could be the use of the heteroassessment tool administered to the parents to observe behavior ascribable to precursors of inattention and hyperactivity disorder in their children

This study is part of a longitudinal researchintervention that has engendered attention, in parents and teachers, towards preterm birth so far little considered.

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PLOS ONE

## A Scoping Review of Interventions to Supplement Spoken Communication for Children with Limited Speech or Language Skills

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#### Abstract

**Background:** Augmentative and Alternative Communication (AAC) is used for treating children with severe disorders of speech-language production and/or comprehension. Various strategies are used, but research and debate on their efficacy have remained limited to a specific area and have rarely reached the general medical community.

Objective: To systematically evaluate outcomes of AAC interventions in children with limited speech or language skills.

Methods: Searches were conducted (up to December 2012) in the MEDLINE, EMBASE, PsycINFO, CINAHL, DARE, and Cochrane Library databases. Furthermore, relevant journals were searched by hand. References from identified studies were examined. Only RCTs were considered. Trial quality was assessed according to a standardized and validated set of criteria.

Results: Fourteen of 1661 retrieved papers met inclusion criteria. A total of 666 children were included in the review and 7 papers involved only children <5 years old. Papers were of average quality and all but one had been published during the previous 10 years by one of 8 research groups, 5 of which from the United States. Seven studies directly addressed AAC use by children with different disabilities. Seven studies enrolled typically developing children: 5 evaluated the use of AAC technologies by children without disabilities in order to obtain results that could be used to improve interventions in peers with disabilities, and 2 evaluated peers' attitudes towards children who used AAC. Both interventions and outcome measures varied widely between studies. Overall findings demonstrate the effectiveness of the AAC interventions considered, but the focus on RCTs alone appears too restrictive.

Conclusions: Solid evidence of the positive effects of AAC interventions in children with severe communication disorders must be generated, and different methods are needed besides RCTs. Moreover, it is important that knowledge, research, and debate extend to the medical community in order to ensure clinically effective AAC provision for these children (and their parents).

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#### Introduction

Ever since non-speech communication systems have been employed in individuals with little or no functional speech, Augmentative and Alternative Communication (AAC) interventions have evolved rapidly. The term AAC includes all forms of communication (other than speech) that are used to express thoughts, needs, wants, and ideas in order to supplement spoken or written communication in individuals with severe disorders of speech-language production and/or comprehension [1].

AAC is only one component of Assistive Technology (AT), which is a broad term referring to assistive, adaptive, and rehabilitative devices that assist an individual in functioning in society at a more appropriate and independent level. AT includes wheelchairs, ramps, and TTYs (phone systems for individuals who are deaf), whereas AAC involves multimodal approaches incorporating gestures, vocalizations, signs, orofacial expressions, as well as picture symbols, voice output devices, or other computerbased technologies, based on what is most successful in meeting the complex communication needs of subjects across different settings. Levels of AAC technology can vary from unaided modes, in which no external device is required (sign languages or gestural cueing systems), to aided AAC [1]. The latter includes lowtechnology (alphabet boards, symbol-based topic boards, and communication books or programs) and high-technology aided modes (electronics and computer technologies).

The percentage of people who find it difficult to communicate their needs effectively without help is about 1.2% of the general population [2], while approximately 5% of preschool children may have some form of language impairment or delay [3], and less

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#### AAC in Children with Speech or Language Disability

than 0.1% have severe to profound deafness with onset before language is established [4,5]. While it is generally known that sign language may be a very relevant choice for infants with profound prelinguistic deafness and that its early and full introduction may support development and mental health [6], the existence and relevance of AAC for development in children with communication disorders is less well-known. From 0.3 to 0.6% of children and adolescents may benefit from AAC interventions [7] for a wide variety of communication problems that can be found in association with numerous medical conditions such as autism spectrum disorder, cerebral palsy, intellectual disabilities, and rare genetic syndromes. AAC is described as an important mean to compensate speech, enhance communicative competence, acquire prelinguistic and cognitive skills essential for language development, and facilitate the emergence of speech and language [8-13]. Moreover, it is considered very relevant to quality of life by parents and users [14]. The objective of AAC interventions is the long term development of functional communication and, possibly, of language skills. Reducing the communicative gap is, in fact, a critical step, because when a toddler has a severe language and communication delay, his ability to interact socially, gain information, develop his cognitive potential and learn from the environment is significantly compromised, with dramatic consequences on his global development and an increased risk of behavior problems. Demonstrating the efficacy of interventions in AAC has therefore been a central concern in the field for many years [15-30]. There has also been debate about which outcomes are to be considered relevant [17,18,20,21] and whether the usual criteria for evaluating evidence may be adequate without modifications [22,29]. Conducting efficacy research in AAC poses significant challenges because of the paucity and heterogeneity of the population of AAC users, the transactional and dynamic nature of the communication process, the variability of AAC systems and interventions [17], the importance of generalization and maintenance [20], and the key role of communication partners and of social validation of objectives [17,18], even more so when addressing a pediatric population. AAC candidates may differ significantly in their functioning, even when affected by the same medical diagnosis: intelligence, attention, receptive language, expressive language, adaptive behavior, and motor skills may all be compromised, but to various extents and with different possible combinations. Moreover, communication is a process by which people jointly build meaning [8]. Each partner contributes to the interaction by using language, gestures, eye gaze, body posture, cultural norms, and speech, and the specific characteristics of the communicating partners highly influence the entire process. This, in turn, influences the possible communicative needs of the patient and the shared definition of outcomes [17,18].

Many journal articles involving AAC have been published during the last decade and the number is increasing. A specific journal (the official journal of the International Society for Augmentative and Alternative Communication) has been published quarterly since 1985 and has been indexed since 2005 by the Institute of Scientific Information (ISI). There has also been a marked growth in the publication of books on the topic. Nonetheless, research and debate seem to have remained limited to a very specific area of rehabilitation and have rarely reached the medical community. A better knowledge of AAC and of its possible impact on children and families would be important for guaranteeing timely referral of children and families and therefore improving their quality of life and helping to prevent behavioral problems and cognitive deterioration. Critical points in AAC research methodology may also be considered as an example of the challenges that need to be faced in building solid evidence for

complex interventions with high context involvement in rare diseases.

Efforts to implement evidence-based practice in AAC have been made, also highlighting the importance of properly performed systematic syntheses aimed at determining the effectiveness of interventions in AAC [24-28], despite the fact that data are still scant. The number of AAC intervention studies has increased rapidly and a few randomized controlled trials (RCTs) have also been carried out. Although RCTs are the most rigorous way of determining whether a cause-effect relationship exists between intervention and outcome, the appropriateness of such stringent designs has been questioned for the AAC field [22,29]. Nonetheless, no systematic review of RCTs on outcomes of AAC interventions in children has been carried out, except for one on the effects of AAC on speech production in children with autism. This study which included mostly single-subject experimental design studies and only 2 RCTs, and is now 5 years old [28]. Taking into account the extensive literature on AAC and the range of AAC interventions, a scoping review of RCTs was performed in order to explore the extent of RCT production in AAC, and to help identify target points (population, intervention, comparison, outcomes, and context) for future critical appraisal processes.

#### Methods

#### Search Strategy

An extensive search of the published literature was conducted. The following electronic databases were searched for articles published in any year up to December 2012: MEDLINE, EMBASE, PsycINFO, CINAHL, DARE, and the Cochrane Library. References from identified studies were examined and relevant journals (EBCAI - Exidence-based Communication Assessment and Intervention and AAC - Augmentative and Alternative Communication) were hand searched. The general search strategy used was: [(communication aids for disabled OR facilitated communication)] AND (child§ OR adolesce§ OR pediatr§). The search was performed also using the term "alternative and augmentative communication" as free text. The search terms used were specific to each database, according to the Pearl Growing strategy [28]. Reference lists were searched for potentially relevant articles.

#### Inclusion Criteria

Criteria for inclusion in the review were: (1) participants aged under 18 years; (2) description of a specific AAC intervention; (3) a comparative group was considered; (4) intervention outcomes were specifically reported; and (5) comparisons were randomized and conducted for intervention and control groups.

Studies were excluded from the review if: (1) participants were aged more than 18 years or insufficient detail was provided to ascertain participant age; (2) outcome assessment was not reported; (3) a specific intervention was not assessed; or (4) the study did not utilize a randomized controlled design.

#### Data Extraction and Assessment

All identified abstracts were manually read for their applicability to inclusion and exclusion criteria and potentially relevant articles were obtained and examined. All references retrieved were collected and analyzed using the Reference Manager v.11 program (Institute for Scientific Information, Berkeley, California, USA). Articles meeting inclusion criteria were examined to extract the following information: sample characteristics (age range, clinical characteristics, sample size); experimental and control interventions; outcomes and method used to measure the

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outcomes, inclusion and exclusion criteria, developmental measures, mean IQ, communication and language measures, and mean communication level at baseline. References of pertinent papers were also scrutinized for additional relevant articles. Study quality of RCTs was assessed using the Delphi list [31].http://adc. bmi.com/content/95/9/717.full - ref-19 This tool includes items relating to whether: randomization was conducted, treatment allocation was blinded, participant groups differed at baseline, and intention to treat analysis was conducted. Total scores are unweighted and ranged from 0 (poor quality) to 9 (high quality). Each study was also assessed using the Jadad point scale [32]. The instrument contains 3 items related directly to reduction of bias (randomized, double-blind, and withdrawals and drop outs), and 7 additional items (in the present evaluation) to check for other markers (objectives, outcome measures, inclusion and exclusion criteria, sample size, interventions, control group, and statistical analysis). Total scores ranged from 0 to 10. Both authors assessed each of 13 pertinent randomized studies independently, and interreviewer disagreement was solved by discussion. Agreement on inclusion was calculated using the Kappa statistics.

#### Results

#### Search Results

The literature search resulted in 1661 titles. A total of 543 duplicates and 1008 non-pertinent or non-appropriate references were deleted, resulting in 110 potentially relevant articles. Authors agreed on 90 of 110 papers (81.8%) selected for reliability check (K = 0.633), and disagreements were resolved by consensus. Thirty-nine studies (35.4%) met inclusion criteria and were controlled studies. Of these, 14 were randomized and were therefore included in the final step of the review (figure 1) [33-46].

The 110 pertinent articles were published between 1983 and 2012, with 26 (23.6%) published before 2000. In 2004 the number of papers published increased and the yearly rate remained steady since then. These papers appeared in 50 different journals, 33 of which published only 1 paper each (30%). Only 10 journals published at least 3 papers each, for a total of 45 papers (44.1%). The articles were published by 342 authors, most of whom (76.9%) appeared in 1 paper each, and only 13 of whom (3,8% of all authors) appeared in at least 3 papers. These 13 authors belonged to one of 7 groups (4 American and 1 Australian, 1 Italian, and 1 South African) and produced 32 of the pertinent papers (29.1%). The study by Wu et al. [34] was considered to fall within the scope of AAC and not of deaf education because it was focused on the efficacy of translating icons into written language, a topic that goes well beyond the area of hearing impairment.

#### RCTs Identified

Table 1 summarizes the characteristics of the 14 included trials. All are single-center, randomized controlled studies, performed in 3 countries across 3 continents (Africa, Asia, and North America). Eleven of the studies (78.6%) were from USA [33,35–40,42,44– 46] and, specifically, from 5 groups. These groups reported the results (usually as a thorough examination) of the approach they developed. All RCTs were published in the last 10 years, except one published in 1988 [33], and were published in 7 different journals. Six of the journals had an impact factor and the average was 2.64 (1.18–5.01). One journal did not have an impact factor [41].

**Participants.** Seven studies regarded children with disabilities [33–39] and seven involved typically developing children [40– 46]. The latter were, nonetheless, included in the review because they evaluated ways to improve or support interventions in peers

with disabilities. One of the studies on children with disabilities regarded profoundly deaf children whose associated disabilities were not described [34]. As mentioned before, this study was included because it involves research on augmentative communication technologies to translate icons into written language. In the studies regarding children with disabilities, the number of children involved ranged from 10 to 68 (median 36), with a total of 299 children included. Three studies referred to the same patients [35-37]. The ages of the 227 children ranged from 1.5 to 16 years, with a mean of 4.6. Five trials involved only children (157/227; 69.2%) less than 5 years old [35-39]. Six studies [33,35-39] reported both developmental level/IQ at baseline (mean DQ/IQ between 40 and 60) and communicative level (mean expressive language between 9.9 and 21.5 months; mean receptive language between 14.1 and 20 months). One of the studies [34] did not report the developmental/cognitive level of the children enrolled nor their communicative competence at baseline, but reported literacy level (mean 73) because the study described an intervention aimed at improving literacy in deaf children. Table 2 reports additional details on participant characteristics.

Five studies [40–44] involving typically developing children regarded ways of improving the learn ability of AAC systems, and involved between 20 and 60 children (median 46), with a total of 208 children included. The children's ages ranged from 2.3 to 6.9 years (mean 4.9). Two trials involved only children less than 5 years old (50/208 children; 24%) [40,42].

The other 2 studies [45–46] regarded peer attitudes towards AAC users, and the number of children involved ranged from 95 to 136 (median 115), with a total of 231 children included. The children's ages ranged from 7 to 18 years (mean 13.1).

Children with a history of developmental delay, learning, hearing, or uncorrected vision problems, or in whom the local language (English or Africaans) was not the mother-tongue of the child, were excluded from all 7 studies involving typically developing children.

Study-Quality Assessment. The Delphi score ranged from 2 to 5 (mean 4.0), with 9 as the maximum possible score. No studies concealed the treatment allocation or completely blinded the outcome assessor, the care provider, or the patient.

The Jadad score ranged from 3 to 8 (mean 5.1), with 10 as the maximum score possible. No studies were described as doubleblind, and only one justified the sample size [44]. Only 1 study described withdrawals and drop outs [41] and 8 the statistical analysis methods used [33,35–37,40,41,44–46].

Outcome assessment. The outcome measures used in the 14 studies differed widely. Of the 7 studies [33-39] in which efficacy of AAC interventions was tested in children with disabilities, one involved joint attention during communication, object exchange turns and requests [35], and the generalization of use of symbols [37], one regarded the increase in target vocabulary and communicative interactions [38], one the improvement in reading comprehension [34], and one the parents' attitudes following intervention [39]. Four studies' outcomes included speech directly (number of spoken words during treatment [33], number of different child-initiated spoken words during the training sessions [35], number of non-imitative spoken acts and different words [36], or increase in target vocabulary [38]). In 5 studies [40-44] AAC technologies were used in typically developing children without disabilities, in order to compare different training levels and types of tools used or of interventions performed, and to use results to improve interventions in peers with disability. In 2 studies [45,46] outcome measures were focused on the attitudes of typically developing children towards

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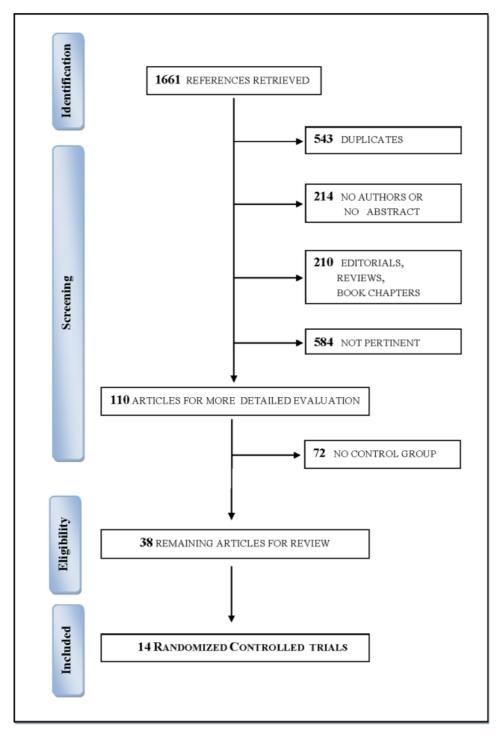


Figure 1. Flow chart of the search strategy used for identification and selection of trials. doi:10.1371/journal.pone.0090744.g001

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| Author Age group  |   |   |   |   |              |
|---|---|---|---|---|--------------|
| (year) in years<br>country (mean) No                            | Intervention  | Comparative<br>group  | Outcome<br>measure  | Key outcome<br>findings   | Delphi score |
| in children with disability who use                             |   |   |   |   |              |
| Yoder & <9 (5.4) 60<br>Layton<br>(1968) [33]<br>USA             | 90 individual training<br>sessions of 40 minutes<br>(min) each alternating<br>sign and speech   | Children trained with<br>sign alone: with speech<br>alone, or with<br>simultaneous sign<br>and speech | Total number of<br>different child-<br>words during the<br>training sessions  | Training conditions<br>that included verbal<br>of verbal output and the expectation<br>of verbal output were<br>superior to sign alone in<br>facilitating sportrameous<br>spoken words during<br>treatment  | 29           |
| Wu et al. 11.0- 10<br>(2004) [34] 16.0 (13)<br>Taiwan           | Three months training<br>with a Chinese text<br>generating computerized<br>program based on a<br>predictive sentence<br>template  | Children trained<br>with the conventional<br>teaching method  | The literacy aptitude<br>test and subjective<br>satisfactory level  | The literacy aptitude<br>test and subjective<br>satisfactory level<br>improved significantly<br>(~40%)  | 2            |
| Yoder and 1.8- 36<br>Stone (2006) 4.5 (2.8) (19+17)<br>[35] USA | Picture Exchange<br>Communication System<br>(PECS) 20 minute therapy<br>sessions, 3 times per week<br>for 6 months (72 sessions),<br>and up to 15 hrs of parent<br>training | Responsive Education<br>and Prelinguistic Milleu<br>Teaching (IRMT)                                   | Rating scale of<br>coded variables<br>during Early Social<br>Communication<br>Scales (ESCS)<br>Play with Examiner<br>(UFPE), and parent-<br>sessions<br>sessions  | The RPMT facilitated<br>the frequency of<br>generalized turn taking<br>and generalized turn taking<br>and generalized point<br>attention more than<br>did the PECS. However,<br>in children with very<br>little joint attention<br>generalized requests<br>more than RPMT                                 | v            |
| Yoder and 1.8- 36<br>Stone (2006) 4.5 (2.8) (19+17)<br>[36] USA | Picture Exchange<br>Communication System<br>(PECS) 20 minute threapy<br>sessions, 3 times per week<br>for 6 months and up to<br>15 hrs of parent training                   | Responsive Education<br>and Prelinguistic Milleu<br>Teaching (RPMT)                                   | Systematic analysis<br>of larguage<br>transcripts to count<br>the frequency of<br>nonimitative spoken<br>nonimitative spoken<br>records of examiner-<br>child free play<br>assorics hand<br>counting of different<br>nonimitative words,<br>counting of different<br>nonimitative words,<br>play coder software<br>play coder software<br>play coder software<br>different toys<br>touched. | Children who started<br>intervention with high<br>object exploration<br>increased the number<br>of nominative words<br>fare with REPMT. However,<br>the opposite was true<br>with REPMT. However,<br>the opposite was true<br>for children who<br>started intervention<br>with low object<br>exploration. | v            |
|   |   |   |   |   |              |

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| Author<br>(year)<br>country                  | Age group<br>in years<br>(mean)              | No | Intervention  | Comparative<br>group   | Outcome<br>measure  | Key outcome<br>findings  | Delphi score |
|--|--|----|---|--|---|--|--------------|
| Yoder and<br>Lieberman<br>(2010) [37]<br>USA | 1.5-<br>5.0 (3.1)                            | *  | Picture Exchange Responsive Education<br>Communication System (PECS) 20 and Preingustic Milleu<br>minute therapy Teaching (RPMT)<br>sessions, 3 times a week for<br>6 months (72 sessions), and<br>up to 15 his of parent<br>training   | Responsive Education<br>and Preinguistic Milleu<br>Teaching (RPMT)                 | Mean m° of picture<br>exchanges during<br>ESCS-Abridged                           | The mean n° of<br>picture exchanges<br>for PECs and RPMT<br>groups were 3.84<br>and 1.01, respectively   | m            |
| Romski et al<br>(2010) (38]<br>USA           | 1,7-<br>33 2.5)                              | 8  | Pirent-coached augmented<br>communication in pur and<br>parent-coached augmented<br>communication output, 24<br>sessions of 30 min each,<br>in three 10 min blocks<br>(play, book reading, and<br>snads) in which anget<br>social in which anget<br>sessions were in laboratory<br>sesting and 6 in child home,<br>distributed over a median<br>of 15–16 with | Parent-coached spoken<br>communication<br>intervertion                             | Augmented words<br>and spoken words<br>use: communication<br>interaction skills   | Vocabulary size was<br>substantially larger for<br>AAC interventions<br>than for spoken<br>communication<br>intervention   | *            |
| Romski et al.<br>(2011) [39]<br>USA          | 1.6-3.3<br>(2.5)<br>31-45<br>Parents<br>(37) | r, | Parent-coached augmented<br>communication input and<br>parent-coached augmented<br>communication output, 24<br>parent-coached augmented<br>communication output, 24<br>parente of min blocks<br>(play, book reading, and<br>snack) in which rarget<br>snack in which anget<br>sections were in laboratory<br>secting and 6 in child home,<br>of 15-16 wks     | Parent-coached spoken<br>communication<br>intervention                             | The 20 Items of the<br>Parent perception of<br>language<br>development<br>(PPOLD) | More positive<br>perceptions of<br>success after all<br>interventions.<br>Interventions,<br>language difficutities<br>language difficutities<br>language difficutities<br>language difficutities<br>language difficutities<br>severity of the ACC<br>intervention. | Ť            |
| Studies on typically developing children     | loping children                              |    |   |  |   |  |              |
| Drager et al.<br>(2004) [40]<br>USA          | 3.0-<br>3.9 (3.5)                            | 8  | Use of dynamic display<br>with 61 vocability items,<br>in a contextual scene<br>format 4 learning sessions<br>(30 min each) and 1<br>generalization session   | Participants in the grid-<br>single-symbol and grid-<br>single shot menu condition | The children's accuracy in locating target vocabulary                             | Children performed<br>significantly better<br>with AAC<br>technologies in a<br>contextual scene format<br>than in a grid format,<br>but by the fourth<br>session the diffrence<br>was no longer<br>significant   | 4            |
|  |  |    |   |  |   |  |              |

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| Author<br>(year)<br>country                            | Age group<br>in years<br>(mean)   | Ň       | Intervention  | Comparative<br>group   | Outcome<br>measure  | Key outcome<br>findings  | Delphi score |
|--|---|---------|---|--|---|--|--------------|
| Basson and<br>Alant<br>(2005) [41]<br>South Africa     | 6.0-<br>6.9 (5.4)   | \$      | Exposure and one session<br>training with a thematically-<br>organized communication<br>overlay with (Picture<br>Communication<br>Symbols <sup>1M</sup> (PCS) | Children receiving<br>exposure only and no<br>training   | The accuracy of<br>children's selection<br>of the symbol in<br>response to its<br>spoken label,<br>representing the<br>symbol's<br>gue sability                                     | The 16 PCS symbols<br>had an iconicity of<br>12-2-25% and there<br>was a significant<br>improvement in the<br>second session.<br>greater in the trained<br>group   | m            |
| McCarthy<br>et al. (2006)<br>[42] USA                  | 23-<br>29   | 50      | 3 exposure sessions, 10–<br>30 min each, to<br>redesigned enhanced<br>scanning uechnque to<br>reduce learning demands   | Traditional scanning<br>technique  | The child's accuracy<br>in selecting target<br>items  | The children in<br>enhanced scanning<br>condition were more<br>than twice as accurate<br>in their scanning<br>performance at their<br>peers in the traditional<br>scanning condition   | 4            |
| Alant et al.<br>(2010)<br>(43)<br>South Africa         | 5.1-<br>6.9 (5.8)   | 8       | Sequential exposure to<br>different types of colored<br>meaningful symbols  | Sequential exposure to<br>different types of<br>colored arbitrary forms<br>of 3 color conditions | The accuracy and<br>rate with which the<br>participants<br>identified the items<br>in a stimuli anay  | The sequential exposures<br>condensings) impacted<br>both on time and<br>accuracy for meaningful<br>accuracy for meaningful<br>instances   | 4            |
| Schlosser<br>er al.<br>USA (44)                        | 3-3.10<br>(3.6.hildren)<br>3.11-4.9<br>(18.children)<br>4.10-5.8<br>(1.8.children)<br>(4.3) | 22      | Animated representation<br>of 24 verbs and 8<br>setail prepositions from<br>the ALP Animated<br>Graphics Set  | Static representation of<br>prepositions from the<br>ALP Animated Graphics<br>Set                | Effect of symbol<br>format animated,<br>static), of word class<br>(verb, preposition),<br>and of age (3, 4,<br>5 yrs dd) on<br>tansarency, name<br>agreement, and<br>identification | Animation effect was<br>significant for<br>transparency, but not<br>for name agreement<br>and identification.<br>The effect was more<br>pronounced for verbs<br>than prepositions, and<br>older children<br>outperformed younger<br>children | *            |
| Studies on peer attitudes towards children who use AAC | es towards children   | who use | AAC   |  |   |  |              |
| Beck et al.<br>(2003) (45)<br>USA                      | 7–8<br>30 children)<br>9–10<br>(31 children)<br>11–12<br>(3.4 children)<br>(9.6)            | 8       | A school-based<br>educational program<br>providing information<br>and a 16 min video<br>regarding AAC, in<br>combination with a<br>role-play experience       | Children receiving<br>information and video<br>alone   | The 26 items of the<br>Assessment of<br>Attitudes Toward<br>Augmentative and<br>Alternative<br>Communication<br>(AATAAC) scale  | A greater positive<br>effect of the information<br>plus role-play experience<br>compared to the effects<br>of being given<br>information alone for<br>older children and boys  | 4            |

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| ble 1. Cont.                       |   |     |  |                                      |  |  |              |
|------------------------------------|---|-----|--|--------------------------------------|--|--|--------------|
| thor<br>ar)<br>intry               | Age group<br>in years<br>(mean)   | ۶   | In tervention  | Comparative<br>group                 | Outcome<br>measure   | Key outcome<br>findings  | Delphi score |
| k et al.<br>10) [46]               | 14 yrs           15 dolescents)           15 yrs           16 yrs           16 yrs           17 yrs           (20 adolescents)           17 yrs           (20 adolescents)           17 yrs           (8 adolescents)           18 yrs           (15.6) | 136 | 8 videotapes depicting 4<br>different gender<br>combinations of AAC<br>communication<br>partners, a dynamic touch<br>screen device | AAC users with a static touch screen | The 33 items of the<br>Assessment of<br>Attitudes Toward<br>Autimetative and<br>Alternative and<br>Communication-2<br>(AATAAC-2) scale | Type of AAC device<br>combined with<br>familiarity with people<br>with disability and<br>gender contribute to<br>adolescents' attrude<br>towards people who<br>use AAC | un .         |
| 10.1371 /Journal.pone.0090744.t001 | ne.0090744.t001   |     |  |                                      |  |  |              |

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peers who use AAC, as a possible relevant aspect of communication partners' interaction with users.

Details of group designs of the randomized controlled trials involving children with disabilities are reported in Table 2.

Yoder & Layton [33] tested the main, and interaction, effects of 4 different training conditions (alternating presentation of sign and speech, sign alone, speech alone, and simultaneous presentation of sign and speech) and of pretreatment elicited verbal imitation ability in predicting child-initiated spoken language use during training sessions of minimally verbal autistic children less than 9 years old. Training conditions that included verbal input and the expectation of verbal output were superior to sign alone in facilitating spontaneous spoken words during treatment, and pretreatment verbal imitation ability positively predicted the size of the child-initiated spoken vocabulary. Exploratory analysis indicated that pretreatment age and IQ may also predict spoken language development during training.

The Wu et al. study [34] proposed a computerized, graphic interface based on a predictive sentence template tree for translating icons of Taiwanese sign language into Chinese written sentences, and compared it with a conventional teaching method in children with profound hearing impairment in the fifth grade of a primary school for the deaf in Taiwan. Findings showed an improvement rate in Chinese reading comprehension in deaf children in the intervention group. The proposed system applies the design methodology of sentence prediction and construction to develop the task or domain-specific sentence types.

The study by Yoder & Stone [35] compared the relative efficacy of two communication interventions, Responsive Education and Prelinguistic Milieu Teaching (REPMT), and Picture Exchange Communication System (PECS), on initiating joint attention, on object exchange turns, and on requests, in 36 preschoolers 18–60 months of age with autism spectrum disorders and less than 10 spoken words. In autistic children with some joint attention, REPMT facilitated the frequency of generalized turn taking more than PECS, while the opposite occurred in children who began the study with no joint attention.

The second article by Yoder & Stone [36] regarded the same research, but considered spoken communication acts as outcomes. The growth rate of different, spoken, nominative words was faster in the PECS group than in the REPMT group for children who began treatment with relatively high object exploration, while the opposite occurred for children who began treatment with low object exploration.

The Yoder and Lieberman [37] study, by the same authors [35,36], represented an extension of the previous studies, focusing on the generalization of use of symbols. The study found that young children with autism who received PECS training increased the number of picture exchanges to a greater extent than children receiving REPMT, when in a controlled context that was different from the training context in several dimensions. PECS use may thus be one way to help a child not only to begin to use joint attention towards objects and people, but also to use it to communicate in generalized contexts.

Romski et al [38] compared three parent-coached language interventions (augmented communication input and output and spoken language intervention) in young children 24–36 months old with developmental delays who began with fewer than 10 spoken words, and found that augmented language interventions increased target vocabulary and communicative interactions to a greater extent than spoken communication interventions. The authors concluded that AAC does not hinder, but actually aids, speech production abilities in young children with developmental delay, and does so even over a short period of time. They state that

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more research is needed on the interaction between comprehension and production of augmented and spoken words, and that this interaction appears to be more complex than was initially hypothesized.

Finally, the study by Romski et al [39] focused on parental perceptions of language development in toddlers from the previous study [38], demonstrating that augmented language intervention also has a positive impact on parental perception of language development in their children. Both studies highlight the important role AAC interventions can play at a very early age for children who are having difficulties with speech and language development.

The Drager et al. study [40] investigated the learning demands of different AAC dynamic displays in typically developing 3 year old children. Results showed that, initially, transparency was poor for all AAC technologies used, but participants performed better across successive sessions. By the second learning session, children in the contextual scene-screen shot condition performed significantly better than children in the two grid conditions, but by the fourth session the difference was no longer significant. Embedding language concepts within contextual scenes may be an effective approach for young children learning dynamic display AAC technologies. However, authors conclude that the systems differed by more than one characteristic and the performance of typically developing children may not be fully generalizable to that of older children or children with disabilities. Moreover, functional use in free play remained low, confirming the importance of better exploring the different effects of support provided in order to facilitate learning, generalization, and spontaneous use.

The Basson and Alant study [41] set out to determine how accurately typically developing, 6 year old, urban, Africaans speaking children who had at been enrolled for at least 6 months in preschool could identify 16 Picture Communication Symbols (PCS), with and without training. Results confirmed that a rather low percentage of symbols can be correctly identified on first exposure based only on iconicity. A significant improvement at retest, although greater in the intervention group, was seen in both experimental and control groups, showing that iconicity may be only one of the components that facilitate the learning and memory of AAC symbols, and that exposure and training also play a relevant role. The number of participants and of symbols considered was limited, and again performance of typically developing children may not be fully generalizable to that of children with disabilities. The authors therefore conclude that different symbols, different grid sizes, different ages and cultural groups, and different training strategies need to be considered in future studies.

The purpose of the McCarthy et al. study<sup>42</sup> was to investigate the learning demands of a redesigned scanning technique and to compare it with traditional scanning in typically developing 2 year olds. Results indicate that, after three learning sessions, most typically developing 2 year olds increase their accuracy with the redesigned scanning technique further than with traditional scanning. However, results may not be generalizable to children with disabilities, and other scanning designs and the development of new and innovative access techniques need to be investigated.

The Alant et al. study [43] examined the role of color on rate and accuracy in identifying symbols in typically developing children. Findings indicate that the use of different colored symbols in sequential exposures impacts the time and accuracy of symbol location, and contributes to understanding how typically developing children locate different types of symbols in a context in which the color of symbols changes. The findings confirm both the complexity of factors affecting visual search and processing and the fact that understanding visual search processes requires a sound analysis of the multiple factors embedded in the process within a specific task or context.

In the study by Schlosser [44] et al, the effect of animation on transparency, name agreement, and identification of graphic symbols for verbs and prepositions was evaluated in typically developing preschoolers of 3 age groups. The animation effect was significant for transparency, but not for name agreement or identification. The effect was more pronounced for verbs than prepositions. A developmental effect was observed for each measure. The authors suggested that there is a need to replicate the study with different symbol sets, with child directed control of animation, and with additional symbols on the display. In the Beck et al. study [45] typically developing children in 2nd, 4th, and 6th grade of a small suburban elementary school with no children with disabilities in their class were given one information session on peers using AAC, alone or combined with role playing, in order to evaluate possible changes in their attitude towards these peers. In the group of older children and, particularly, in boys, the association of a role-playing experience resulted in higher positive self-reported attitude scores toward peers who use AAC than did the provision of information alone. The authors conclude that, even though a change in attitude does not necessarily imply a change in behavior, determinants of children's attitudes towards their peers who use AAC and of formation of friendships between them need to be explored further.

The second study from Beck et al [46] is similar to the previous one [45] and is aimed at investigating elements of high school students' self-reported attitudes towards peers who use AAC. The study found that the type of AAC device, along with familiarity with people with disabilities and gender, contribute to adolescents' attitudes towards people who use AAC.

#### Discussion

To our knowledge, this is the first scoping review to investigate outcomes of AAC interventions that focuses only on RCTs and uses a standardized set of criteria for the assessment of the methodological quality and strength of evidence of retrieved RCTs studies. Previous reviews also considered other study designs, such as non randomized group studies [23–25] or single case experimental designs [20,24–26,28], and therefore used a broader approach for selecting papers for the review [47].

The results of the retrieved studies, while providing some information on the effects of AAC interventions, confirm numerous limitations in the use of RCTs to evaluate AAC interventions:

- a) all trials were described as randomized, but the risk of bias was unclear in the majority of studies because the methods of random-sequence generation and allocation concealment were not explicitly reported;
- b) non-uniform formal reporting of outcome results reduced the power of findings and their communication to readers;
- c) the comparison groups used in the reviewed studies differed in the criteria employed, both within and between studies, potentially causing bias because no concealed randomization was used;
- none of the included studies used a random selection strategy or a case-controlled design, so the quality score could not exceed 5, despite the highest potential score of 9;
- e) all included studies had relatively small sample sizes, especially 4 of the studies enrolling patients with disabilities (10 in one study and 36 in the other three) [34–37]. Only

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| Author<br>(year)<br>country              | Inclusion<br>criteria  | Exclusion<br>criteria                            | Developmental<br>measures                    | Mean IQ (SD)<br>at baseline  | Communication<br>and language<br>measures  | Mean<br>communication<br>level (SD) at<br>baseline  |
|--|--|--|--|--|--|---|
| Yoder &<br>Layton<br>(1988) (33)<br>USA  | <9 yrs old   | -hearing or<br>vision deficits                   | Leiter or Bayley<br>or Merril-Palmer         | Mean nonverbal IQ<br>42.9 (17.8); 40.5<br>(33.1); 41 (23.8);<br>44.4 (24.4)                                  | Expressive and<br>receptive scales<br>of Sequenced<br>Inventory of<br>Communication<br>Development<br>(SCID);  | Mean receptive<br>language 17.3<br>(6.7); 14.1 (4.2);<br>14.9 (5.9); 16.2<br>(4.1)                |
|  | -Autism or PDD-<br>NOS: CARS score<br>between moderate<br>and severe |  |  |  | parent<br>questionnaire<br>of initial<br>expressive<br>vocabulary;   | Expressive language<br>15.2 (12.6); 9.9<br>(6.9); 12.3 (6.5);<br>11.7 (8.8)                       |
|  | -expressive and<br>receptive age <28<br>months (mths) on<br>SICD     |  |  |  | experimenter<br>designed<br>instrument for<br>elicited verbal<br>imitation   | Initial vocabulary<br>6.8 (7.3); 4.8 (7.1);<br>6.5 (7.6); 3.9 (7.9)                               |
|  | -expressive vocabulary<br><25 words on parent<br>questionnaire       |  |  |  |  | Elicited verbal<br>imitation 298.1<br>(342.2); 281.5<br>(321); 258.6<br>(348.1); 287.7<br>(360.7) |
| Wu et al.<br>(2004)<br>[34]<br>Taiwan    | -profoundly deaf<br>students   | - not reaching<br>prerequisite<br>literacy level | not reported                                 | not reported   | Literacy<br>aptitude test  | Mean literacy level:<br>73 (8.12); 73 (5.7)   |
|  | -fifth grade   |  |  |  |  |   |
|  | -primary deaf<br>school<br>in Taiwan                                 |  |  |  | Semantic<br>integration<br>index per<br>utterance  | Mean Semantic<br>integration level:<br>0.42 (0.10); 0.41<br>(0.13)                                |
| Yoder and<br>Stone<br>(2006) [35]<br>USA | -Autism or PDD-<br>NOS at ADOS                                       | -severe sensory<br>or motor deficits             | Mullen scales<br>of early learning<br>(MSEL) | Mean MSEL<br>composite score<br>of 55 (7) for PECS<br>and 54 (6) for<br>RPMT (children<br>under 49 excluded) | Mulien scales<br>of early learning<br>(MSEL). McArthur<br>Communicative<br>Development<br>Inventories<br>(CDI), Early<br>Social<br>Communication<br>Scales (ESCS),<br>unstructured free<br>play with examiner (UFPE) | CDI: mean words<br>understood 108<br>(87) for PECS and<br>62 (49) for RPMT<br>ESCS and UFPE:      |
|  | -18-60 mths  | -English not<br>primary language<br>at home      |  |  |  | - mean n° of<br>children initiating<br>joint attention: 3 (4)<br>in PECS and 2 (2)<br>in RPMT;    |
|  | -<10 words   |  |  |  |  | <ul> <li>mean n° of objects<br/>exchanges: 5 (5) for<br/>PECS and 2 (β) for<br/>RPMT</li> </ul>   |
|  | -hearing screening ok  |  |  |  |  |   |
| Yoder and<br>Stone<br>(2006) [36]<br>USA | -Autism or PDD-<br>NOS at ADOS                                       | -severe sensory<br>or motor deficits             | Mullen scales<br>of early learning<br>(MSEL) | Mean MSEL<br>composite score<br>of 51 (5,3)<br>(children under<br>49 were<br>assigned 48)                    | Mullen scales<br>of early learning<br>(MSEL).  | SFPE: - mean n° of<br>nonimitative spoken<br>acts 0.25 (0.84)                                     |

Table 2. Group designs of randomized controlled trials involving children with disability who use AAC.

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| Author<br>(year)<br>country                  | Inclusion<br>criteria  | Exclusion<br>criteria                         | Developmental<br>measures                    | Mean IQ (SD)<br>at baseline   | Communication<br>and language<br>measures   | Mean<br>communication<br>level (SD) at<br>baseline                             |
|--|--|---|--|---|---|--|
|  | -18-60 mths  | -English not<br>primary language<br>at home   |  |   | Fifteen minute<br>semistructured<br>free play with<br>examiner (SFPE),<br>Developmental<br>play<br>assessmentTum<br>taking procedure  | - mean n° of<br>different<br>nonimitative word<br>0.17 (0.56)s                 |
|  | -<20 words   |   |  |   |   | -mean n° of<br>communication acts<br>8.4 (10.5)                                |
|  | -hearing screening ok  |   |  |   |   |  |
| Yoder and<br>Lieberman<br>(2010) [37]<br>USA | -Autism or PDD-<br>NOS at ADOS   | -severe sensory<br>or motor<br>deficits       | Mullen scales<br>of early learning<br>(MSEL) | 50.32 (5.2)<br>PECS, 51.76<br>(5.41) RPMT                                   | Mullen scales<br>of early learning<br>(MSEL). MArthur<br>Communicative<br>Development<br>Inventories<br>(CDI), Early<br>Social<br>Communication<br>Scales (ESCS),<br>unstructured free<br>play with<br>examiner (UFPE)            | Mullen expressive<br>language score:<br>19.47 (1.26 PECS,<br>21.59 (3.36) RPMT |
|  | -18-60 mths  | -English not<br>primary language<br>at home   |  |   |   | Mullen receptive<br>language score:<br>19.26 (0.45) PECS,<br>19.41 (0.51) RPMT |
|  | -<10 words   |   |  |   |   |  |
|  | -hearing screening ok  |   |  |   |   |  |
| Romski et al.<br>(2010) [38]<br>USA          | -24-36 mths  | -autism                                       | Mullen scales<br>of early learning<br>(MSEL) | Mean MSEL<br>composite score<br>of 60 for AC-1<br>and 59 for AC-0<br>and SC | MSEL<br>expressive and<br>receptive scales,<br>McAnhur<br>Communicative<br>Development<br>Inventories,<br>Sequenced<br>Inventory of<br>Communication<br>Development<br>and Clinical<br>Assessment of<br>Language<br>Comprehension | Receptive language<br>18 mths;<br>20 mths; 19 mths                             |
|  | -<10 intelligible<br>spoken words  | -deafness/hearing<br>impairment               |  |   |   | Expressive<br>language 12 mths;<br>13 mths; 13 mths                            |
|  | -score of less than<br>12 mth on<br>expressive language<br>scale of MSEL | -delayed speech<br>and language<br>impairment |  |   |   |  |
|  | -at least primitive<br>communication<br>abilities                        |   |  |   |   |  |
|  | -motor skills that<br>permitted the child<br>to touch the symbols        |   |  |   |   |  |
|  | - English as primary<br>language at home                                 |   |  |   |   |  |

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| Author<br>(year)<br>country        | Inclusion<br>criteria | Exclusion criteria      | Developmental<br>measures                    | Mean IQ (SD)<br>at baseline  | Communication<br>and language<br>measures  | Mean<br>communication<br>level (SD) at<br>baseline |
|------------------------------------|-----------------------|-------------------------|--|--|--|--|
| Romski et al.<br>2011) [39]<br>JSA | As in previous study  | As in previous<br>study | Mullen scales<br>of early learning<br>(MSEL) | Mean MSEL<br>composite score<br>of 60 for AC-1<br>and 59 for AC- 0<br>and SC | MSEL<br>expressive and<br>receptive scales,<br>McArthur<br>Communicative<br>Development<br>Inventories,<br>Sequenced<br>Inventory of<br>Communication<br>Development<br>and Clinical<br>Assessment of<br>Language<br>Comprehension | Receptive language<br>18 mths; 20 mths;<br>19 mths |

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three studies [33,38,39] on children with disabilities enrolled a slightly greater sample (60, 68, and 53 children): the two most recent were by Romski et al. [38,39]. The larger samples regarded the two studies by Beck et al [45,46] (95 and 136 children, respectively), in both cases regarding typically developing children's attitudes towards peers using AAC. Comparing such relatively small groups might also be a potential cause of bias;

- f) most of the reviewed studies explored different AAC techniques or even single components of the technique, making comparison between studies very difficult;
- g) the outcomes evaluated differed between studies and also within individual groups [35–37].

Because the entire group of retrieved RCTs was characterized by entirely different study outcomes, no attempt was made to aggregate these outcomes across studies. Similarly, effect size estimation was not used since studies differed substantially in design features and quality.

AAC intervention is a long term, complex, multimodal process that needs to be incorporated into daily life. It includes prescription, development, and customization of AAC systems to meet the unique needs of each user; instructions for the individual who uses AAC in various linguistic, operational, social, and/or strategic skills following various instructional protocols; instructions for facilitators in interaction strategies to reduce opportunity barriers and support effective communication; and instructions for facilitators in the operation, maintenance, and ongoing development of the AAC systems used [8,20,23]. Furthermore, each one of these intervention components involves multiple procedures. Most of the published studies were focused on separate effects of single components of AAC intervention, while the intervention itself is, in fact, a multidimensional process whose ultimate effect may be quite different from the sum of its components. In this context, group designs are difficult to implement because of the small AAC population and the wide variability within it. Children have complex communication disorders, arising from different medical diagnoses, which may lead to differing disabilities. Enrolled populations range in age from infancy to late teens,

and vary widely in functional profiles such as movement, cognition, communication, receptive and expressive language, learning characteristics, vision, and hearing. They also vary in their educational setting (mainstream schools or special education), previous and concurrent interventions, and concurrent medical conditions. In addition, children will experience different social relationships and interact with many different people in many different environments. Each of these factors will influence communication and interventions, especially since communication is a process by which people build shared meaning. Correcting for the effect of these variables in RCTs is extremely difficult. Moreover, AAC intervention increases the complexity of human interaction and acts on several specific domains. The effects of intervention may therefore have an impact on a wide variety of behaviors, and outcomes in one domain may influence outcomes in other domains without the possibility of separating out the effects. In the UK Medical Research Council's (MRC) definition [48], interventions are considered to be complex when there is a high number of components and interactions within the experimental and control environments, in the number or difficulties of behaviors required by those delivering or receiving the intervention, in the number of groups or organizational levels targeted by the intervention, in the number and variability of outcomes, or in the degree of flexibility or tailoring of the intervention permitted, and AAC interventions fully fit the definition.

Due to the above limitations, it has been argued that RCTs are not first line in complex interventions [48] and that they are possibly not appropriate for AAC research involving individuals with disabilities [17,19–22]. Results of the present systematic review on RCTs seem to confirm these authors' conclusions. Some of the critical points in obtaining adequate evidence in AAC have, in fact, already been analyzed by various authors, and solutions suggested [16–23,27–30], but these have somehow remained confined to specific journals and the debate has not reached the general medical literature. The single subject experimental design (SSED) is considered to be a relevant design option in AAC [28], and is, in fact, widely used in the field. SSED considers each subject as his-her own control, and methodologies for analyzing, in detail, the quality of SSED and for synthesizing the results of

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various studies through meta-analysis have been developed for AAC [22,29], and a different hierarchy of evidence has been proposed [22]. However, other alternatives should also be considered, since the quasi-experimental research design could be an appropriate approach and should be tested in the AAC field [19]. In particular, the most commonly used design, the nonequivalent groups design, which substitutes statistical "controls" for the physical control of the experimental situation through a pre-test/post design, should be used. The design is the same as the classic controlled experimental design except that the subjects cannot be randomly assigned to either the experimental or the control group, and the researcher cannot control which group will get the treatment. Participants do not all have the same chance of being in the control or the experimental groups, or of receiving or not receiving the treatment. Such a design could potentially be a better adjusted approach to evaluate the efficacy of interventions in children with complex disabilities.

Randomized studies remain the gold standard when enrolling typically developing children, involving either ways of improving the learnability of systems in order to make them more developmentally sensible or interventions aimed at modifying peer attitudes towards AAC users. A significant number of subjects can be more easily reached, and randomization can be employed, when addressing these populations, and the use of non disabled subjects in AAC research has therefore been widely discussed [48-50]. Typically developing children may be enrolled to evaluate symbol acquisition, interaction abilities, selection techniques, speech generating device usability, perception of communicative competence, and language acquisition. Nonetheless, the RCTs retrieved regarded only symbol acquisition, speech generating device usability, and peer attitudes. In the first two situations, the main question concerns external validity: the performance of typically developing children can provide interesting suggestions for future research and development, but it may not be fully generalizable to a population of people who are communicatively impaired. Moreover, the outcomes analyzed in the studies retrieved appear to be partial and very limited when compared to the outcomes expected from AAC interventions. Learnability of a few isolated symbols over a very short period of time is, in fact, very different from using hundreds of various symbols in the long term and in fully functional, everyday communication exchanges, and probably implies very different underlying mechanisms and motivation.

The third situation could be more promising for future research development. Up to now, the majority of the research on interventions has focused on evaluating modifications in the behaviors of AAC users rather than in their conversational partners, while it is known that partners play a key role not only in communication skill acquisition, but also in generalization and maintenance [21]. Studies on the training of conversation partners could reach larger numbers of subjects (each child has many conversation partners) and could more easily be randomized. Larger numbers would also permit an analysis of the effects of different components, namely the impact of having an adult or a child as a partner, the different relationships influencing children (parents, siblings, grandparents, other family members, teachers, classmates, etc), and the role of gender, educational level, previous training, and present communication style. Nonetheless, as found by the studies included in this review, RCTs are very limited and not of optimal quality, making this an area of research that needs significant effort.

Blinding appears to be another relevant point in AAC research. While blinding of the subject, the family, and the interventionist is next to impossible, blinding of the assessor is generally feasible and should be pursued and reported.

Given the extreme variety of subjects that are candidates for an AAC intervention, as much detailed information as possible should be provided regarding the above mentioned patient characteristics (age, cognitive level, receptive and expressive language, attention, behavioral phenotype, previous AAC experience, type of school placement, full diagnosis including comorbidity, etc) in order to determine in whom the intervention was successful and to permit replication of findings. Most tests that explore neuropsychological functions have been created and standardized for typically developing children, and require the integrity and integration of other functions in addition to the one evaluated. This may lead to an underestimation of the extent to which functioning is not homogeneous between children, particularly when considering subjects with severe motor or intellectual disabilities. The homogeneous reporting of subject characteristics and the identification of more appropriate and shared instruments for evaluation [53] are very relevant topics for future evolution [19,50-52].

AAC research has many interesting components. Communication is one of the fundamental human rights, and its impairment results in significant consequences in various areas of child development. Lack of functional communication is generally a life-long condition that severely impacts quality of life of subjects and their families, and is highly correlated with subsequent behavioral problems and high social and economic costs. Access to AAC interventions is still an unmet need in most countries; the few studies available [2,4,54-56] report from 22 to 60% of children not receiving any AAC intervention, depending on the years considered and on the geographical area. The main barriers identified are resource availability issues (lack of funding, limited access to AAC equipment, etc) and lack of training, and time available, of professionals. Service development and access, as well as the set up of complex interventions and their evaluation appears to be more critical in developing countries and in non Englishspeaking countries due to linguistic, cultural, and socioeconomic reasons. The results of this review confirm that interest in, and willingness to face, the challenge of evaluating interventions is still limited to a few research groups (mainly American), with a longstanding experience in the matter, suggesting that production and acquisition of "evidence" in the field needs further effort and participation. Time and resources are needed for guaranteeing all children in need of ACC interventions efficacy-proven, accessible techniques, since up to now these needs have remained neglected for the majority of patients.

None of the retrieved RCTs were multicenter studies, suggesting that intergroup collaboration is difficult in the area, also due to the different complexities of AAC patients and, possibly, to linguistic differences between countries. However, collaborative studies are efficacious approaches that favor the transferability of acquired knowledge into common practice, overcoming difficulties and converging on intervention choices. This type of study therefore represents an achievement in the AAC field.

AAC intervention evaluation also represents an interesting example of complexity [48], with similarities to research in rare diseases. The identification of valid and reliable outcome measures appears critical. Possible changes are, in fact, multidimensional, and in order to be measured they need different tools in different domains (language comprehension, symbol and language use, functional communication, cognitive development and learning, participation and inclusion, quality of life, decrease in negative behavior, child and family satisfaction, etc) and require more long term evaluations. The interactive nature of the communication

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process makes the participation of users, family members, facilitators, teachers, and professionals particularly important in defining objectives. Different people of different ages and with different roles, however, may lead to different outcomes, so social validation techniques need to be included from the start, when the research question is defined, and not at the end of studies. This could be an issue of significant relevance in research in the field of complexity [17,18,48]. As in most complex interventions, an improvement in transparency and quality of reporting is also a very relevant topic for future development [17,24,48,57] for all study designs. A better understanding of the different contexts in which an intervention is applied, as well as of the different possible ways of implementing it that can preserve intervention integrity, is essential [58,59], as is the clear description of the intervention theory base, modeling of components, outcomes, pilot testing, and process of evaluation alongside the clinical trial. Criteria proposed by Mohler et al. [60] appear interesting and consistent both with the methods of development recommended by the EQUATOR network and with previous discussions on the topic in the AAC field.

#### Conclusions

Solid evidence of the positive effects of AAC interventions in children with severe communication disorders still needs to be generated. The efficacy of interventions in AAC remains a central concern because of the scant evidence, and the debate has mostly remained limited to specialized literature and has not reached the general medical field. Efficacy research in AAC poses significant challenges due to the paucity and heterogeneity of the population of AAC users, the transactional and dynamic nature of the communication process, the variability of AAC systems and interventions, the importance of generalization and maintenance, the key role of communication partners and of social validation of

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objectives, and the impact of different languages and cultures on the transferability of results. The low quality of the randomized controlled studies analyzed in this review confirm both the complexity of evidence-building in this field and the fact that studies based on different methodologies are needed in addition to RCTs. No evidence of any harmful effects of AAC in children with speech and language difficulties and their families has, however, been found, and positive trends in communication were shown. With access to appropriate assistive technology at the early stages of development, young children with complex communication needs may be able to maximize their language and communication development and achieve their full potential. Additional research (collaborative and multicenter), designed in innovative ways that can address the complex, multifactorial aspects of the field, as well as studies of higher methodological quality, are therefore urgently needed.

Moreover, it is important that knowledge, research, and debate extend to the medical community in order to ensure clinically effective AAC provision for these children (and their parents).

#### Supporting Information

Checklist S1 PRISMA Checklist. (DOCX)

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#### Author Contributions

Conceived and designed the experiments: MB. Performed the experiments: MB MAC, Analyzed the data: MB MAC, Wrote the paper: MB MAC.

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## La sintomatologia ADHD come fattore di rischio per lo sviluppo di condotte alimentari patologiche in adolescenza: uno studio longitudinale

## ADHD symptoms as risk factors for dysfunctional eating habits in adolescents: results from a longitudinal study

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**RIASSUNTO. Scopo.** Obiettivo di questa ricerca è quello di indagare la relazione tra sintomi di disturbo da deficit dell'attenzione/iperattività (ADHD) in infanzia e adolescenza e il successivo sviluppo di condotte alimentari problematiche. **Meto**di. Il campione oggetto di indagine è composto da 217 adolescenti (maschi: 30,9%; età media: 17,1 ± 0,88; range: 16-19 anni) reclutati nel comune di Parma nel contesto di un disegno di ricerca longitudinale della durata di 8 anni che prevedeva tre valutazioni (T1-T2-T3). Tutti i partecipanti sono stati sottoposti, al T1 (età media: 12 anni) e al T2 (età media: 14 anni), a un'intervista strutturata finalizzata alla rilevazione, nell'attualità e nell'arco della vita, di sintomi riconducibili all'ADHD e, al T3 (età media: 17 anni), a un'intervista per la rilevazione di condotte alimentari patologiche (digiuno, condotte di eliminazione, BMI). Sono state condotte analisi correlazionali e regressioni tra i punteggi relativi ai vari domini sintomatologici dell'ADHD e agli indici raccolti al T3 relativi alle condotte alimentari disfunzionali. **Risultati**. I dati suggeriscono che le associazioni tra ADHD e comportamenti alimentari disfunzionali risentono di differenze legate al genere: nelle femmine la sintomatologia ADHD rilevata al T2 risulta predittiva di condotte di eliminazione, mentre nei maschi essa è predittiva del sovrappeso rilevato al T3. **Discussione**. La sintomatologia ADHD, a prescindere dal superamento della soglia diagnostica, può condurre ad adottare condotte alimentari costiche e poco organizzate che possono indurre, nelle femmine, alla messa in atto di condotte di eliminazione, e nei maschi, a un incremento ponderale.

PAROLE CHIAVE: ADHD, condotte alimentari disfunzionali, studio longitudinale

SUMMARY. Aim. The aim of this study is to analyze the relationship between attention deficit hyperactivity disorder (AD-HD) symptoms in childhood and early-adolescence and the development of dysfunctional eating habits later in life. The sample under investigation is composed of 217 adolescents (males: 30.9%; mean age: 17.1 ± 0.88 ys; range: 16-19 ys) voluntarily recruited in the city of Parma (Northern Italy) in the context of a longitudinal research project focused on developmental factors of antisocial behaviour. All subjects were assessed at T1 (mean age: 12 ys) and at T2 (mean age: 14 ys) using a structured clinical interview to collect information on ADHD symptoms on a lifetime basis and, at T3 (mean age: 17 ys), they were administered an interview to assess pathological eating habits. Correlation and regression analyses were carried out between scores of the three symptom domains of ADHD and eating habits as assessed at T3. Results suggest that the association between ADHD symptoms and eating habits show differences according to gender, in that in females ADHD symptoms assessed at T2 are associated with compensatory behaviours, while in males they are predictive of overweight as assessed at T3. ADHD symptoms, although under threshold, may lead to chaotic and unorganized eating habits which might put female at risk for compensatory behaviours and males for overweight.

KEY WORDS: ADHD, dysfunctional eating behaviour, longitudinal study.

## INTRODUZIONE

Il disturbo da deficit di attenzione/iperattività (ADHD) è oggi tra i disturbi comportamentali dell'infanzia e dell'adolescenza più frequentemente diagnosticati e si manifesta con un quadro sintomatologico che include deficit attentivi, iperattività e impulsività (1). Benché sia ampiamente riconosciuto che i soggetti con ADHD sperimentino una serie di difficoltà in adolescenza che includono problemi nella relazione con i genitori e con i coetanei, scarso rendimento scolastico, problemi emotivi, problemi di condotta e consumo di sostanze (2-6), pochi studi hanno indagato il possibile rapporto intercorrente tra ADHD e sviluppo di condotte alimentari disfunzionali e franchi disturbi del comportamento alimentare (DCA). È da rilevare che la mancanza, fino a tempi recenti, di ricerche volte a considerare la possibile relazione esistente tra ADHD e condotte alimentari patologiche è da attribuire prevalentemente alla forte preponderanza dei soggetti di genere maschile nella letteratura sull'ADHD e alla focalizzazione sullo studio dei bambini piuttosto che degli adolescenti (7).

Tuttavia, dal momento che i soggetti che manifestano comportamenti di alimentazione incontrollata e condotte di eliminazione sono caratterizzati da elevati livelli di impulsività (8), la possibilità che i soggetti con ADHD, e in primo luogo le femmine, siano a maggiore rischio di condotte alimentari disfunzionali non è da sottovalutare.

Alcune recenti ricerche che si sono mosse in questa direzione, condotte sia su campioni clinici sia su campioni estratti dalla popolazione generale, forniscono dati a favore dell'esistenza di un possibile legame tra sintomi di ADHD e sviluppo di condotte alimentari patologiche, in particolare tra le femmine.

Un ampio studio (9) effettuato su più di 2000 pazienti ricoverate per DCA ha rilevato tassi di ADHD più elevati rispetto alla popolazione generale nel caso delle pazienti affette da bulimia nervosa (BN) (9%), ma non nel caso delle pazienti con anoressia nervosa (AN), sottotipo restrittivo (3%). Surman et al. (10) hanno esaminato la presenza di BN in un campione di bambini e adolescenti (di età compresa tra i 6 e i 17 anni) e in un campione di adulti di entrambi i sessi, con o senza ADHD, rilevando una prevalenza di BN significativamente più elevata nelle donne affette da ADHD (11,2%), se paragonate a quelle senza ADHD (2%), ma non hanno riscontrato alcuna differenza tra gli uomini adulti e tra i bambini di entrambi i sessi. Cortese et al. (11) hanno preso in considerazione la presenza di sintomi di ADHD e di comportamenti bulimici in un campione clinico composto da 99 adolescenti di entrambi i

sessi gravemente obesi, di età compresa tra i 12 e i 17 anni. I ricercatori hanno rilevato che gli adolescenti con comportamenti bulimici presentavano con maggiore probabilità anche sintomi di ADHD, e in particolare disattenzione e impulsività, indipendentemente dai punteggi relativi alle misure di ansia e depressione. L'associazione tra DCA e ADHD è stata confermata sia in studi trasversali effettuati su campioni di adolescenti con condotte alimentari problematiche (12) sia in campioni di adolescenti con disturbo da deficit dell'attenzione (13), sia in studi longitudinali, Mikami et al. (14) hanno effettuato uno studio prospettico su un diverso campione di soggetti composto da 432 adolescenti con ADHD/sottotipo combinato e 264 ragazzi di controllo di entrambi i sessi: gli adolescenti con ADHD/sottotipo combinato mostravano più sintomi di BN rispetto ai ragazzi di controllo e, tra i soggetti con ADHD/sottotipo combinato, le femmine manifestavano con più probabilità comportamenti bulimici rispetto ai maschi; erano i sintomi di impulsività rilevati in infanzia a predire i sintomi di BN in adolescenza, in particolare tra le femmine. Biederman et al. (15), in uno studio prospettico della durata di 5 anni effettuato su un campione composto da 235 ragazze adolescenti con o senza ADHD, hanno dimostrato che le ragazze con ADHD manifestavano una probabilità 3,6 volte maggiore di sviluppare un DCA rispetto al gruppo di controllo e, nello specifico, 5,6 volte più probabilità di manifestare BN e 2,7 volte più probabilità di sviluppare AN.

Alcuni casi clinici hanno messo in luce un effetto del metilfenidato nel ridurre la frequenza degli episodi di alimentazione incontrollata e la messa in atto di condotte eliminatorie in soggetti con BN che manifestavano sintomi di ADHD (16-18). Tali risultati sostengono l'ipotesi che il trattamento farmacologico dei sintomi di impulsività, connessi all'ADHD, possa risultare utile anche per migliorare il quadro sintomatologico della BN. Infine, uno studio (19) effettuato su un campione di soggetti con ADHD ha rilevato un tasso di prevalenza maggiore, rispetto a quello riscontrato tra i soggetti di controllo, dei DCA e in particolare del disturbo di alimentazione incontrollata.

Ricerche trasversali e longitudinali hanno messo in luce anche l'esistenza di un possibile legame tra ADHD e obesità (20-23), per quanto i risultati appaiano controversi. Mentre questi studi hanno messo in luce un aumento del rischio di obesità negli individui che presentavano sintomi di ADHD, altri hanno dimostrato che la prevalenza di sovrappeso nei soggetti con ADHD non risultava maggiore rispetto a quella rilevata tra i soggetti di controllo (15,24).

L'obiettivo di questo contributo è verificare l'esistenza di un legame tra sintomi di ADHD e condotte

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alimentari patologiche in adolescenza, in particolare tra le femmine. Nello specifico, nel presente studio è stata indagata la relazione esistente tra sintomi di ADHD nlevati a 12 e 15 anni e il successivo sviluppo di condotte alimentari patologiche e di incremento ponderale all'età media di 17 anni. L'idea di analizzare la presenza di un disturbo come l'ADHD all'interno di un campione tratto dalla popolazione generale trova il suo sostegno nel punto di vista di quegli autori (25,26) che ritengono utile considerare ogni disturbo non solo da un punto di vista categoriale, ma anche dimensionale. La scelta di indagare il fenomeno in esame mediante un disegno di ricerca prospettico-longitudinale è riconducibile al fatto che tale metodologia permette di analizzare l'associazione tra un fattore di rischio precoce e l'insorgenza di un determinato outcome in epoche successive e quindi, a differenza dei disegni di ricerca di tipo trasversale, consente di inferire relazioni di tipo causale.

## MATERIALI E METODI

#### II campione

Il presente contributo si è sviluppato nel contesto dello SLAP (Studio Longitudinale sugli Adolescenti di Parma). un progetto di ricerca longitudinale avviato nella città di Parma nel 2001 e che ha previsto la somministrazione di interviste e questionari in tre tempi diversi (T1, T2, T3). Nel corso del T1 (2001-2002) sono stati intervistati 579 studenti, a un'età media di circa 12 anni (media=12,01; DS=±0,47; range: 11-13), rappresentativi dell'intera popolazione di adolescenti iscritti alle scuole medie inferiori di Parma; i risultati relativi alla prevalenza di ADHD rilevata in questa prima fase della ricerca sono stati illustrati in un precedente contributo (27). 534 (92,2% del campione iniziale) adolescenti hanno poi partecipato al T2 (2004-2006) all'età media di circa 15 anni (media=14,71; DS=±0,45; range: 14-15 anni). La fase di rilevazione del T3 (2007-2009) ha coinvolto 217 soggetti (37,5% del campione iniziale), 150 femmine (69,1%) e 67 maschi (30,9%), di età media pari a circa 17 anni (media=17,1; DS=±0,88; range: 16-19 anni).

Per quanto al confronto tra il campione al T1 e al T3 sia stato rilevato un cambiamento significativo nella proporzione tra i due generi (con una riduzione significativa nella prevalenza di maschi;  $\chi^2$  corretto per la continuità=37,27; gl=1; p<0,001), nessuna differenza è stata rilevata tra coloro che sono stati sottoposti alle tre valutazioni e tutti gli altri, quando confrontati rispetto all'intensità media della sintomatologia ADHD rilevata al T1. A tale proposito è stata condotta un'analisi della covarianza che ha mostrato che né l'aver o meno partecipato al T3, né il genere, né la loro interazione hanno un effetto sul punteggio medio relativo alla sintomatologia ADHD al T1. La partecipazione alla ricerca è avvenuta su base volontaria, attraverso il coinvolgimento delle scuole e previa sottoscrizione di un apposito modulo di consenso informato da parte dei genitori o di chi esercitasse la patria potestà sul minore.

L'elevato tasso di dropout nel campione è imputabile al fatto che, mentre tutti gli istituti di scuola media inferiore di Parma avevano offerto la loro disponibilità a collaborare alla ricerca (permettendo agli operatori di condurre le interviste direttamente all'interno dell'istituto), lo stesso non è avvenuto per gli istituti superiori.

#### Gli strumenti

La presenza dei sintomi di ADHD è stata indagata per mezzo di interviste diagnostiche strutturate differenti nei due tempi: al T1 è stata somministrata la Diagnostic Interview for Children and Adolescents (DICA-R) (28) e al T2 la Diagnostic Interview Schedule for Children (DISC-IV) (29). Si tratta, in entrambi i casi, di interviste volte alla formulazione della diagnosi dei principali quadri clinici con esordio in età evolutiva, seppure la DICA-R si basi sui criteri diagnostici del DSM-III-R1 (30), mentre la DISC-IV è stata elaborata sulla base dei criteri DSM-IV (31). Inoltre, risultano diversi gli intervalli temporali indagati; infatti, nel caso dell'intervista DICA-R al soggetto viene chiesto di rispondere a ciascuna delle domande facendo riferimento sia a qualsiasi momento del passato, sia all'attualità, mentre nel caso della DISC-IV le domande sono formulate esclusivamente rispetto all'attualità. Considerando nel complesso le informazioni raccolte a partire dalle due interviste è stato possibile ricavare due variabili relative all'ADHD:

- ADHD T1-lifetime, rilevata a 12 anni, ma riferita anche a un'epoca precedente attraverso il ricorso alla DICA-R; tale variabile è ottenuta dalla somma del punteggio relativo ai 14 item e ha una consistenza interna pari a 0,780 (a di Cronbach). Al soggetto è stato chiesto di rispondere a ogni domanda esprimendo il proprio grado di accordo o disaccordo su una scala Likert con un punteggio da 1 a 5 ("1" corrisponde a "mai" e "5" a "sempre");
- ADHD T2-attualità, rilevata a 15 anni mediante la DISC-IV. Tale variabile si riferisce a una scala composta

<sup>&</sup>lt;sup>4</sup>La versione riveduta della teiza edizione del DSM (30) ha proposto l'ipotesi di un disturbo unitario in cui i sintomi venivano presenta ti in un'unica lista di 14 di cui almeno 8 dovevano essere presenti per poter formulare la diagnosi; in questo modo viene impedita la possibilità di formulare diagnosi di sottotipi specifici del disturbo a seconda del prevalere di configurazioni sintomatologiche peculiari. Tale approceio trovava una sua gluttificazione nell'assenza di chiate evidenze empiriche circa le dimenzioni di base a cui ricondurre ciascui sintomo e circa la legittinità del numero-soglia di sintomi da soddisfare per giungere alla formulazione della diagnosti. Il DSM-IV (31) ha mantenuto la medesima etichetta diagnostica ma ha inserito criteri differenti e ha accolto la possibilità di clusterizzare i sintomi proponendo tre aree: deficit dell'attenzione (9 sintomi), iperattività (6 sintomi) e impulsività (3 sintomi).

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da 22 item che ha una consistenza interna pari a 0,855 (KR-20) e include item a risposta dicotomica (sì-no).

Si è inoltre deciso di suddividere la sintomatologia rilevata nel T1 e nel T2 nelle tre dimensioni di: disattenzione. iperattività e impulsività; se tale ripartizione è implicita nei criteri del DSM-IV (e quindi per i dati relativi a DISC-IV), per quanto riguarda i dati raccolti mediante DICA-R ci si è basati sulle indicazioni provenienti dalla letteratura (1). Tale scelta appare giustificata da due ordini di considerazioni; prima di tutto, l'importanza attribuita in letteratura all'impulsività, più che all'iperattività, nell'eziopatogenesi delle condotte alimentari patologiche di tipo abbuffate e condotte di eliminazione in adolescenza (11,13). In secondo luogo, nessuno dei soggetti inclusi nel campione della presente ricerca risulta soddisfare i criteri per una diagnosi formale di ADHD2, pertanto si è ritenuto opportuno utilizzare indici dimensionali della sintomatologia sotto-soglia sulle tre aree che caratterizzano il disturbo. Si sono quindi ottenute tre variabili relative al T1 e riferite al passato: disattenzione T1-lifetime (5 item,  $\alpha = 0.660$ ), iperattività T1-lifetime (6 item. a=0.521) e impulsività T1-lifetime (3 item, α=0.337) e tre variabili relative al T2 disattenzione T2-attualità (11 item, KR-20= 0,829), iperattività T2-attualità (6 item, KR-20=0,570) e impulsività T2-attualità (5 item, KR-20=0.517).

La valutazione relativa alle condotte alimentari patologiche è stata eseguita al T3 attraverso un'apposita sezione della Boricua Child Interview (BCI) (32) relativa alla Scala dei Disturbi Alimentari. La BCI è un'intervista composta da 270 quesiti, che permette di raccogliere informazioni relative a temperamento, tratti di personalità, condotte comportamentali ed eventi che hanno segnato la vita dell'adolescente. La Scala dei Disturbi Alimentari permette la raccolta delle informazioni necessarie al calcolo dell'indice di massa corporea e quelle relative alle abitudini alimentari del soggetto. Una prima sezione indaga il ricorso a strategie finalizzate alla perdita di peso o a evitare di ingrassare, che costituiscono forme di alimentazione problematica: digiunare (ovvero non ingerire cibi solidi per almeno 24 ore), procurarsi il vomito, assumere lassativi o altri tipi di farmaci per evitare di ingrassare; la seconda permette invece di rilevare la presenza e la frequenza di alcuni comportamenti, pensieri e modi di sentirsi che possono costituire segnali di allarme in un'ottica di prevenzione della patologia alimentare, come la costante paura di essere sovrappeso, la consapevolezza delle calorie contenute nei cibi, la tendenza a evitare di assumere carboidrati e il senso di colpa dopo aver mangiato.

Gli item inclusi nella prima sezione sono quattro, e nello specifico: "Hai mai provato a perdere peso digiunando?", "Ti sei mai procurato/a il vomito per dimagrire o evitare di ingrassare?", "Hai mai fatto uso di lassativi per dimagrire o per evitare di ingrassare?" e "Hai mai assunto farmaci specifici per dimagrire o per evitare di ingrassare?".

A partire dai dati raccolti mediante la BCI, sono stati quindi costituiti i seguenti indici: esperienze di digiuno, condotte di eliminazione (che include gli item 2,3,4 della prima sezione;  $\alpha$ =0,558). I 12 item che compongono la seconda sezione della Scala dei Disturbi Alimentari sono stati integrati a costituire un indice cui ci si riferirà con "segnali di allarme" ( $\alpha$ =0,897). Infine, avendo rilevato il peso e l'altezza dei soggetti, è stato possibile ricavare per ognuno l'indice di massa corporea (body mass index, BMI) al T3.

### RISULTATI

È stata prima di tutto valutata l'entità della correlazione esistente, all'interno del campione totale, tra il punteggio dimensionale relativo alla sintomatologia ADHD rilevata al T1 (riferita all'arco di vita) e al T2 (riferita all'attualità) e le variabili riguardanti le abitudini alimentari patologiche e il BMI rilevati al T3 (**Tabella 1**).

Come è possibile osservare, all'interno di questo campione la variabile ADHD rilevata al T1 non correla in modo significativo con nessuna delle variabili concernenti le abitudini alimentari disfunzionali rilevate al T3 né con il BMI. Al contrario, la variabile ADHD rilevata al T2 correla in modo significativo con i tentativi di perdere peso mediante digiuno ( $\tau$ =0,154) e con le condotte eliminatorie ( $\tau$ =0,148) rilevate al T3. Considerata l'importanza che il genere gioca nel caso dello sviluppo delle condotte alimentari patologiche, si è deciso di analizzare separatamente le correlazioni tra ADHD e variabili di interesse nei maschi e nelle femmine.

|                      | Digiuño<br>T3 | Condotte<br>eliminatorie T3 | Segitali di<br>allaritte T3 | BMI T3 |
|----------------------|---------------|-----------------------------|-----------------------------|--------|
| ADHD T1<br>Lifetime  | -0,10         | 0,082                       | 0,007                       | 0,047  |
| Disattenzione T1     | 0,013         | 0,095                       | -0,014                      | -0,055 |
| Iperattività T1      | -0,011        | 0,065                       | 0,052                       | -0,001 |
| Impulsività Ti       | -0,058        | 0,007                       | -0,024                      | 0,068  |
| ADHD T2<br>Attualità | 0,154*        | 0,148*                      | 0,061                       | 0,067  |
| Disattenzione T2     | 0,154*        | 0,147*                      | 0,082                       | 0,082  |
| Iperattività T2      | 0,130*        | 0,068                       | 0,008                       | 0,056  |
| Impulsività T2       | 0,128*        | 0,173**                     | 0,055                       | 0,036  |

<sup>&</sup>lt;sup>2</sup>Ricordiamo che la prevalenza di ADHD rilevata al T1 (DSM-III-R) era risultata pari all'1,2% (n=570) con un rapporto maschi/femmine pari a 1.5:1 (27). Il fatto che il campione attuale non includa nessuno dei soggetti che, al T1, presentassero una forma clinicamente rilevante di ADHD rappresenta, come verrà meglio approfondito in seguito, un limite della presente ricerca.

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Come è possibile osservare nella Tabella 2, nel caso Tabella 3. Correlazione (r di Kendali) tra ADHD e condotte delle femmine la variabile ADHD rilevata al T1, e riferita all'arco di vita, non correla in modo significativo con nessuna delle variabili concernenti le abitudini alimentari disfunzionali rilevate al T3 e con il BML Al contrario, la variabile ADHD rilevata al T2 correla in modo significativo con i tentativi di perdere peso mediante digiuno (r=0,148) e con le condotte eliminatorie (π=0,170) nlevate al T3.

Analizzando nel dettaglio quali dimensioni dell'ADHD rilevata al T2 correlassero con le condotte alimentari patologiche rilevate al T3 tra le femmine, dopo aver scomposto la variabile ADHD T2 nelle tre dimensioni di disattenzione, iperattività e impulsività, è osservabile come la variabile digiuno risulti significativamente correlata alla disattenzione ( $\tau = 0,149$ ), ma non all'iperattività e all'impulsività.

Nel caso delle condotte eliminatorie rilevate a 17 anni, disattenzione (r=0,164) e impulsività (r=0,213) hanno mostrato una correlazione significativa, a differenza dell'iperattività. È stata quindi effettuata una regressione multipla stepwise, inserendo come variabili indipendenti le due dimensioni dell'ADHD rilevate al T2 (disattenzione e impulsività) e come variabile dipendente le condotte di eliminazione rilevate al T3. La regressione ha mostrato che la sola impulsività risulta predittiva delle condotte eliminatorie (β=0,261; p<0,01) e il modello finale è risultato statisticamente significativo (R<sup>2</sup>=0,077; F<sub>(2,142)</sub>=5,932; p<0,01).

Osservando la Tabella 3, è possibile rilevare l'esistenza di una correlazione tra la sintomatologia ADHD rilevata al T1 (π=0,264) e al T2 (π=0,320) e incremento del BMI a 17 anni. In particolare, indagando il ruolo giocato indipendentemente da disattenzione, iperattività e impulsività in questo legame, è stato pos-

|                      | Digiuño<br>T3 | Condotte<br>eliminatorie T3 | Segnali di<br>allaritte T3 | BMI T3 |
|----------------------|---------------|-----------------------------|----------------------------|--------|
| ADHD T1<br>Lifetime  | -0,037        | 0,099                       | 0,021                      | -0,036 |
| Disattenzione Ti     | -0,005        | 0,118                       | 0,039                      | -0,006 |
| Iperattività Ti      | -0,042        | 0,071                       | 0,037                      | -0,077 |
| Impulsività Ti       | -0,085        | 0,002                       | 0,004                      | 0,016  |
| ADHD T2<br>Attualità | 0,148+        | 0,170*                      | 0,068                      | -0,006 |
| Disattenzione T2     | 0,149*        | 0,164*                      | 0,094                      | 0,014  |
| Iperattività T2      | 0,121         | 0,095                       | 0,010                      | 0,020  |
| Impulsività T2       | 0,134         | 0,213**                     | 0,079                      | -0,038 |

|                      | Digiuño<br>T3 | Condotte<br>eliminatorie T3 | Segnali di<br>allarme T3 | BMI T3   |
|----------------------|---------------|-----------------------------|--------------------------|----------|
| ADHD T1<br>Lifetime  | 0,115         | /                           | -0,004                   | 0,264**  |
| Disattenzione T1     | 0,103         | /                           | -0,099                   | 0,185*   |
| Iperattività T1      | 0,079         | /                           | 0,058                    | 0,231**  |
| Impulsività T1       | 0,000         | /                           | -0,096                   | 0,226*   |
| ADHD T2<br>Attualità | 0,162         | /                           | 0,012                    | 0,320*** |
| Disattenzione T2     | 0,168         | /                           | 0,055                    | 0,341*** |
| Iperattività T2      | 0,146         | /                           | -0,071                   | 0,232*   |
| Impulsività T2       | 0,151         | /                           | 0,051                    | 0,223*   |

sibile rilevare, nel caso dell'ADHD al T1, la presenza di una correlazione significativa del BMI con le sottodimensioni disattenzione (τ=0,185), iperattività (τ=0.231) e impulsività (τ=0.226). Nel caso della variabile ADHD rilevata al T2, anche le variabili disattenzione (x=0,341), iperattività (x=0,232) e impulsività (r=0,223) sono risultate significativamente correlate con il BMI misurato al T3 nel caso dei maschi.

Al fine di analizzare il ruolo specifico giocato dai sintomi di disattenzione, iperattività e impulsività in tale relazione si è fatto ricorso alla regressione multipla. Il modello di regressione avente come variabili indipendenti disattenzione, iperattività e impulsività rilevate al T2 e riferite all'arco di vita e come variabile dipendente il BMI misurato al T3 è risultato statisticamente significativo (R<sup>2</sup>=0,240; F<sub>(1,59)</sub>=18,660; p<0,001) mostrando un effetto predittivo della sola disattenzione (β=0,490; p<0,001). Un'altra regressione multipla è stata effettuata inserendo come variabili indipendenti disattenzione, iperattività e impulsività rilevate al T1 e come variabile dipendente il BMI misurato al T3. Nel modello finale (R2=0,099; F(1,61)=6,691; p<0,05), la sola variabile iperattività ha mostrato un effetto significativo (\u03b3=0,314;p<0,05), mentre disattenzione e impulsività sono state escluse.

### DISCUSSIONE

Obiettivo della presente ricerca è stato quello di valutare l'esistenza di un legame tra sintomi di ADHD e condotte alimentari patologiche in adolescenza, in particolare tra le femmine. Nello specifico, nel presente studio è stata indagata la relazione esistente tra sinto-

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matologia ADHD rilevata a 12 e 15 anni e il successivo sviluppo di condotte alimentari patologiche e incremento ponderale all'età di 17.

Un primo dato che emerge è la presenza di correlazioni significative tra l'intensità globale della sintomatologia rilevata al solo T2 (ma non al T1) ed esperienze di digiuno e condotte eliminatorie rilevate al T3 nel campione generale.

A partire da tale rilievo, si è ritenuto opportuno procedere a due analisi distinte delle relazioni tra sintomi ADHD e condotte alimentari disfunzionali in funzione del genere, analizzando anche in maggior dettaglio il ruolo specifico di ciascuna delle tre componenti del quadro clinico (disattenzione, iperattività, impulsività).

Per quanto riguarda le femmine, la sintomatologia ADHD rilevata a 15 anni ha mostrato un potere predittivo sull'insorgenza di condotte alimentari disfunzionali all'età di 17 anni, in particolare sulle condotte eliminatorie. Inoltre, il digiuno per perdere peso è risultato significativamente correlato alla disattenzione, ma non all'iperattività e all'impulsività. Tale risultato può essere spiegato facendo riferimento al fatto che, come rilevato da altri autori (33-35), le condotte alimentari caratterizzate da comportamenti restrittivi nei confronti del cibo risultano spesso associate a inibizione comportamentale ed eccessiva aderenza alle regole, caratteristiche opposte rispetto all'impulsività (36). Al contrario, non solo la disattenzione, ma anche l'impulsività rilevata a 15 anni hanno dimostrato di predire l'insorgenza di condotte di eliminazione all'età di 17 anni. Anche questo risultato si è dimostrato in linea con i dati provenienti dalla letteratura, secondo cui i soggetti che manifestano abbuffate e condotte di eliminazione sono caratterizzati da elevati livelli di impulsività (8,37). I comportamenti di alimentazione incontrollata e le condotte di eliminazione, infatti, possono essere concepiti come esempi di discontrollo degli impulsi (38) e l'impulsività è una componente centrale della BN (39), così come dell'ADHD. Inoltre, la manifestazione di comportamenti impulsivi in domini della vita diversi dall'alimentazione, come per esempio comportamenti antisociali e ricorso a sostanze psicoattive, ha dimostrato di essere in grado di predire l'esordio dei sintomi di BN 9 mesi più tardi in un campione di ragazze adolescenti (40). Il legame tra sintomi di disattenzione e messa in atto di condotte eliminatorie è stato riportato anche in precedenti studi, che hanno dimostrato come i sintomi di disattenzione possano giocare un ruolo nel caso dei comportamenti bulimici (11,12). L'alimentazione compulsiva e la successiva messa in atto di condotte di eliminazione, infatti, può essere vista come un meccanismo compensatorio che il soggetto con ADHD utilizza per controllare la frustrazione associata alle proprie difficoltà attentive e di organizzazione (17). Inoltre, è possibile che i problemi attentivi e i deficit delle funzioni esecutive provochino una difficoltà nell'aderire a un regime alimentare regolare, favorendo lo sviluppo di condotte alimentari disfunzionali (11). Tuttavia, i sintomi di disattenzione, potrebbero essere inquadrabili come effetti piuttosto che come cause dell'alimentazione problematica e, in particolare, della perdita di peso, così come affermano alcuni autori (12,41). Una possibilità di questo tipo potrebbe essere sostenuta nel presente studio dal fatto che, all'interno di questo campione, l'esistenza di una relazione con le condotte alimentari patologiche a 17 anni non è stata riscontrata nel caso dell'ADHD rilevata a 12 anni. Per quanto concerne la variabile segnali di allarme rispetto al rapporto con il cibo, la sintomatologia globale ADHD non ha mostrato un effetto predittivo. L'ADHD rilevata all'età di 15 anni, quindi, sembra predire l'esordio di condotte alimentari patologiche tra le femmine, mentre ha un effetto meno significativo rispetto agli atteggiamenti a rischio nei confronti dell'alimentazione.

Infine, esclusivamente nel caso dei maschi, è stata rilevata una relazione predittiva tra sintomi di ADHD rilevati al T1 e al T2 e incremento di massa corporea misurato al T3. Tale risultato è in linea con precedenti studi secondo cui i soggetti caratterizzati da elevati livelli di impulsività e disattenzione rispetto alle sensazioni interne potrebbero con maggiori probabilità incorrere in episodi di alimentazione incontrollata, che a loro volta potrebbero causare un incremento del BMI (41). In particolare, nel caso dei sintomi di ADHD misurati al T2, nel presente campione la disattenzione ha mostrato un effetto maggiormente predittivo rispetto a iperattività e impulsività. Tali risultati sono in linea con i dati provenienti dalla letteratura, secondo cui i problemi attentivi e i deficit nelle funzioni esecutive potrebbero provocare una difficoltà nell'aderire a un regime alimentare regolare, favorendo lo sviluppo di condotte alimentari caotiche e disfunzionali, che potrebbero quindi condurre al sovrappeso (11). I soggetti con ADHD, inoltre, potrebbero essere maggiormente a rischio di sovrappeso e obesità a causa delle minori opportunità di essere coinvolti in attività sportive strutturate (42).

#### CONCLUSIONI

In conclusione, in questo campione italiano di adolescenti tratto dalla popolazione generale i sintomi di ADHD hanno dimostrato un potere predittivo rispetto allo sviluppo di problematiche dell'alimentazione

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con un effetto differenziale in funzione del genere: essi predicono, infatti, condotte alimentari patologiche tra le femmine e il sovrappeso nel caso dei maschi. Si potrebbe ipotizzare che i sintomi di ADHD possano condurre alla messa in atto di condotte alimentari poco organizzate e caotiche che possono provocare un aumento di peso nel caso dei maschi e il ricorso a digiuno e condotte eliminatorie al fine di prevenire l'incremento ponderale nel caso delle femmine.

Ricerche future dovrebbero auspicabilmente concentrarsi anche su campioni clinici, al fine di approfondire al meglio la possibile esistenza di una relazione tra sintomi di disattenzione, iperattività e impulsività e sviluppo di condotte alimentari disfunzionali in età adolescenziale. Sarebbe inoltre fondamentale valutare il ruolo giocato in questa relazione da altri fattori; le relazioni conflittuali con i genitori e il rifiuto da parte dei coetanei, che spesso caratterizzano i soggetti che presentano sintomi di ADHD, per esempio, potrebbero aumentare il rischio di esordio di condotte bulimiche in età adolescenziale (43,44).

La presente ricerca non è esente da alcuni limiti di carattere metodologico. In primo luogo, è possibile rilevare problemi legati al reclutamento dei soggetti. Il campione oggetto di studio del progetto di ricerca SLAP è stato infatti caratterizzato da un elevato tasso di dropout, imputabile primariamente alle difficoltà nel rintracciare i soggetti nel passaggio da scuola media a scuola superiore, ai possibili cambiamenti di istituto e agli abbandoni scolastici. La riduzione della massa campionaria, peraltro, non ha riguardato equamente maschi e femmine ma è risultata sbilanciata rispetto alla variabile genere; se infatti il campione reclutato al T1 era composto equamente da maschi e femmine, il campione al T3 è risultato composto da una prevalenza di femmine.

Un altro limite riferibile al campione è rappresentato dal fatto che il range di età dei soggetti alla terza rilevazione risulta più ampio rispetto a quello dei due tempi precedenti e ciò risulta principalmente imputabile alle difficoltà riscontrate nel rintracciare i soggetti.

Inoltre, gli strumenti per l'assessment dell'ADHD sono stati modificati nel passaggio dalla prima alla seconda rilevazione. Tale dato acquista particolare rilievo alla luce del fatto che le due interviste rimandano a criteri diagnostici diversi e potrebbe giustificare la non predittività dei sintomi ADHD rilevati al T1 e le condotte alimentari disfunzionali rilevate al T3.

Infine, poiché nessuno dei soggetti inclusi nel campione ha dimostrato di soddisfare una diagnosi di ADHD, il presente lavoro si è basato esclusivamente su indici dimensionali della sintomatologia sottosoglia e non sull'ADHD inteso come entità diagnostica. Emerge senza dubbio la necessità di approfondire l'esistenza di una relazione tra una diagnosi formale di ADHD e lo sviluppo di condotte alimentari disfunzionali all'interno di campioni clinici di adolescenti.

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## Autismo. Commissione Senato approva testo unificato. Ci saranno linee guida e Lea

Il testo varato ieri dalla Commissione Igiene e Sanità accorpa quattro ddl il discussione. Le Regioni dovranno istituire centri di riferimento per la diagnosi tempestiva e stabilire percorsi diagnostici terapeutici e assistenziali. Individuate delle linee guida sul trattamento dei disturbi dello spettro autistico che dovranno essere aggiornate dall'Iss ogni 3 anni.



04 APR - Svolta nella commissione Igiene e Sanità del Senato in tema di autismo. Ieri la XII commissione di Palazzo Madama ha approvato un testo unificato che accorpa i quattro ddl (*344 De Poli, 359 Ranucci, 1009 Venera Padua et al, 1073 Magda Angela Zanoni*) in discussione. Il testo, formato dai 6 articoli, all'articolo 3 richiama esplicitamente l'individuazione delle prestazioni riconducibili ai **Livelli essenziali di assistenza**, erogabili a carico del Servizio sanitario nazionale nei confronti dei soggetti affetti da disturbi dello spettro autistico.

Per l'erogazione delle prestazioni vengono definite delle **linee guida**, che dovranno essere aggiornate ogni tre anni dall'Istituto superiore di sanità sulla base della documentazione scientifica nazionale e internazionale, che hanno a oggetto le raccomandazioni relative agli interventi farmacologici e non farmacologici per il trattamento dei disturbi dello spettro autistico

basate sull'evidenza, per distinte fasce d'età, di soggetti trattati. All'Iss spetterà anche il compito di pubblicare e aggiornare l'elenco degli esperti esterni e dei centri scientifici e clinici che collaboreranno alla redazione delle Linee guida. Prima di ogni approvazione triennale delle linee guida, l'Istituto superiore di sanità dovrà pubblicare il relativo progetto sul proprio sito internet, invitando le istituzioni e le figure professionali coinvolte nell'assistenza a soggetti con disturbi dello spettro autistico a fornire suggerimenti e osservazioni.

In tema di **diritto all'informazione**, il foglietto illustrativo dei prodotti farmaceutici dovrà indicare con chiarezza se il prodotto può essere assunto senza rischio dalle persone affette da disturbo dello spettro autistico.

Le Regioni, poi, si dovranno impegnare ad istituire centri di riferimento con compiti di coordinamento dei **presidi della rete** sanitaria regionale, al fine di garantire la diagnosi tempestiva e dovranno stabilire percorsi diagnostici terapeutici e assistenziali per la presa in carico di minori, adolescenti e adulti con disturbi dello spettro autistico, oltre ad adottare misure idonee al conseguimento dei seguenti obiettivi:

- promuovere la realizzazione sul territorio di servizi gestiti da unità funzionali multidisciplinari per la cura e la riabilitazione delle persone autistiche;

promuovere la formazione sugli strumenti di valutazione e le metodologie validati a livello internazionale, nel rispetto delle linee guida degli operatori sanitari dei servizi di neuropsichiatria infantile, di riabilitazione funzionale e di psichiatria;
promuovere la formazione sulle metodologie di intervento educative, validate a livello internazionale, degli insegnanti che seguono alunni con disturbi dello spettro autistico;

- incentivare progetti sull'educazione sanitaria delle famiglie che hanno in carico persone affette da autismo, per ottimizzare le competenze, le risorse e la collaborazione con i servizi di cura;

- garantire la tempestività e l'appropriatezza degli interventi terapeutici attraverso un efficace scambio di informazioni tra operatori sanitari e famiglie;

- prevedere misure di coordinamento tra i servizi di neuropsichiatria infantile e di psichiatria per garantire la presa in carico e il corretto trasferimento di informazioni nel passaggio all'età adulta;

- rendere disponibili sul territorio strutture diurne e residenziali con competenze specifiche sui disturbi dello spettro autistico in grado di effettuare, insieme ai servizi territoriali, la presa in carico di soggetti minori, adolescenti e adulti;

- promuovere progetti finalizzati all'inserimento lavorativo di soggetti adulti con disturbi dello spettro autistico, che ne valorizzino le capacità.

Infine, entro sei mesi dalla conversione in legge del ddl il ministro della Salute dovrà emanare un decreto di aggiornamento del regime delle **esenzioni** relativo all'autismo.

Giovanni Rodriquez

04 aprile 2014







## Mercoledì, 16 aprile 2014 ore 14,00 - aula Guasti



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

Save the date

## **NEWSLETTER – ADHD**

|                   | PSICOPATOLOGIA E PSICOFARMACOLOGIA IN ETÀ EVOLUTIVA :<br>QUADRI CLINICI E TERAPIA FARMACOLOGICA   |  |   |  |
|-------------------|---|--|---|--|
| EDA DI ISCRIZIONE | <u>Per il personale dell'AO Sant'Anna</u> l'iscrizione viene<br>autorizzata dal proprio responsabile tramite programma<br>informatico TOM.  |  | Come raggiungerci   |  |
|                   | <u>Per i partecipanti esterni</u> le richieste di iscrizione dovranno essere effettuate tramite programma informatico TOM.  |  | Auto  |  |
|                   | Per accedere collegarsi al sito internet aziendale<br>http://www.hsacomo.org/v2/3/catalog/  |  | Dall'autostrada A9: uscire allo svincolo C<br>proseguire lungo via Cecilio, proseguire su via                     |  |
|                   | il corso di interesse ed effettuare la richiesta di iscrizione.   |  | p.zza Camerlata imboccare la via Napoleona. F<br>a pagamento presso l'Autosilo Valmulini.                         |  |
|                   |   |  | Mezzi pubblici<br>Tratte urbane autobus ASF con capolinea all'in<br>Poliambulatorio. E' anche raggiungibile con ' |  |
| H                 |   |  | Ferrovie Italiane dello Stato. Info e orari sui risp  |  |
| S                 | Banca Intesa San Paolo S.p.A. Sede di Como Cod. Filiale<br>7550   |  |   |  |
|                   | CODICE IBAN: IT25L0306910910100000300009 intestato<br>all'A.O. "Ospedale Sant'Anna" di Como - Via Napoleona,<br>60 22100 Como, indicando quale causale del versamento:<br>"Psicopatologia e psicofarmacologia 5 e 12 maggio 2014" |  | Segreteria organizzat   |  |
|                   | f f f   |  | Staff Formazione  |  |
|                   | E' fondamentale l'iscrizione sul sistema TOM e  |  | A.O. "Ospedale Sant'Anna"   |  |
|                   | l'invio della copia del bonifico Bancario e dei   |  | Como  |  |
|                   | seguenti dati indispensabili per l'emissione della  |  | Via Ravona 20 - 22020 San Fermo della E   |  |
|                   | fattura:  |  | Tel. +39 031 585 9413   |  |
|                   | Cognome, nome, Codice fiscale, residenza (Via,  |  | Fax +39 031 585 9858/4163   |  |
|                   | N°, CAP Città, Provincia).  |  |   |  |
|                   |   |  |   |  |
|                   | Il tutto potrà essere inviato o per fax ( 031/5854163) o  |  |   |  |
|                   | per mail (franca.stefanoni@hsacomo.org)   |  |   |  |

ROGRAMMA

I Diritti dell'interessato saranno garantiti in ottemperana alla Decreto Legislativo n.196 del 30.06.2003 - Codice in materia di protezione dei dati personali.

## Premessa

I principali quadri clinici della psicopatologia dell'età evolutiva e relativa terapia pasicofarmacologica.

#### Obiettivi

PRESENTAZIONE DEL CORSO

 $\Rightarrow$  Aggiornamento sui protocolli farmacologi delle sindromi psichiatriche in età evolutiva.

## Destinatari

- $\Rightarrow$  Medici delle seguenti discipline:
- Neuropsichiatri infantili Psichiatri
- Pediatri

 $\Rightarrow$  Psicologi specializzati in

Psicoterapia Psicologia

## Docente

- $\Rightarrow$  Dr. Gabriele Masi Neuropsichiatria INFANTILE
- ⇒ Direttore Unità Operativa Complessa di Psichiatria e PSICOFARMACOLOGIA IRCSS STELLA MARIS - PISA

omo Sud, Paolieda rcheggio

ngresso del Trenord e pettivi siti.

#### tiva

di Battaglia



05 MAGGIO 2014 9:30 Registrazione partecipanti 10:00 La depressione 11:30 Disturbo bipolare 13:00 Pranzo 14:00 Disturbi d'ansia, fobia scolare 15:30 Disturbo ossessivo-compulsivo 17:00 Disturbi di Personalità 18:00 Conclusione prima giornata

#### 12 MAGGIO 2014

| 10:00 | Disturbo oppositivo-provocatorio                        |
|-------|---|
| 11:00 | Disturbo della condotta                                 |
| 11:30 | Deficit di Attenzione e Iperattività                    |
| 12:00 | Disturbi dello spettro autistico                        |
| 13:00 | Pranzo  |
| 14:00 | Psicosi e Sindromi schizofreniche                       |
| 15:30 | Disturbi della condotta alimentare                      |
| 17:00 | Discussione, apprendimento e gradimento<br>del convegno |

18:00 Chiusura del Convegno

#### Azienda Ospedaliera Ospedale S.Anna



## CONVEGNO PSICOPATOLOGIA E PSICOFARMACOLOGIA IN ETÀ EVOLUTIVA: QUADRI CLINICI E TERAPIA FARMACOLOGICA

Responsabile scientifico: Dr. Claudio Cetti Direttore DSM A.O. Sant'Anna Como

5 maggio 2014 Dalle 09.30 alle 18.00

12 maggio 2014 Dalle 10.00 alle 18.00

Aula formazione Monoblocco—piano rialzato Ospedale Sant'Anna Via Napoleona, 60—22100 Como



#### Informazioni ECM

L'Ufficio Formazione dell'A.O. "Ospedale Sant'Anna" di Como è registrato come provider nell'ambito del programma ECM/ CPD di Regione Lombardia.

Ai fini dell'attestazione dei crediti formativi ECM è necessaria la presenza effettiva al 100% della durata complessiva dell'evento formativo e l'esito positivo della verifica di apprendimento.

Secondo le indicazioni contenute nella D.G.R. n. 4776 del 30/01/2013 all'evento sono stati preassegnati n. 10,5 crediti ECM.



## **NEWSLETTER – ADHD**

#### marz 2014

## Relatori della Giornata

Laura Salvoni Direttore USC Neuropsichiatria Infanzia e Adolescenza A.O. Papa Giovanni XXIII di Bergamo Stefano Conte Dirigente Medico USC Neuropsichiatria Infanzia e Adolescenza, A.O. Papa Giovanni XXIII di Bergamo Gianluca Daffi Psicologo USC Neuropsichiatria Infanzia e Adolescenza-A.O. Spedali Civili di Brescia; Università Cattolica di Milan Gian Marco Mazzocchi Psicologo, Università degli Studi di Milano-Bicocca & Centro per l'Età Evolutiva di Bergamo Paola Effedri Dirigente Medico USC Neuropsichiatria Infanzia e Adolescenza A.O. Spedali Civili di Brescia Valeria Renzetti Psicologa USC Neuropsichiatria Infantzia e Adolescenza A.O.Papa Giovanni XXIII di Bergamo Astrid Gollner Presidente AIFA Onlus Lombardia, Associazione Italia Famiglie ADHD Simona Valoti Psicologa Collaboratrice AIFA Antonella Giannellini Ufficio Scolastico Regionale per la Lombardia– Ufficio X Ambito Territoriale di Bergamo

Il Disturbo da Deficit di Attenzione e/o Iperattività (ADHD) è uno dei più frequenti disturbi neuropsichiatrici infantili descritti in letteratura nonostante sia tuttora in Italia sottostimato. È un disturbo caratterizzato da un insieme di sintomi ben definiti quali l'iperattività motoria, l'impulsività e la disattenzione, la cui presenza e gravità possono determinare una grave compromissione della qualità della vita dei bambini e del loro contesto ambientale (famiglia, scuola, ecc...).

Il convegno odierno, con il coinvolgimento di Neuropsichiatri Infantili e Psicologi che si occupano da anni di queste problematicità, vuole fornire una migliore informazione sulla natura, sulle caratteristiche cliniche più importanti del disturbo e sulle possibilità di cura.

L'iniziativa si colloca nell'ambito della formazione prevista dai progetti regionali NPIA. Il progetto regionale sull'ADHD coinvolge 18 centri della NPIA della Lombardia ed ha lo scopo di condividere i percorsi di diagnosi e di terapia tra i diversi centri con la partecipazione dell'Istituto Mario Negri di Milano.

L'evento si rivolge a genitori, insegnanti, educatori, neuropsichiatri infantili, psicologi, logopedisti e terapisti della neuro psicomotricità. La partecipazione è gratuita.

Con il Patrocinio



Convegno organizzato in collaborazione con:





Segreteria Organizzativa: Struttura Ambulatoriale "Borgo Palazzo" Via Borgo Palazzo, 130 24125 Bergamo Telefono 035/390680

Azenda Ospelallera Papa Giovanni XXIII Bolena baskara 🐕 Regione

USC NEUROPSICHIATRIA INFANZIA E ADOLESCENZA

## IL DISTURBO DA DEFICIT **DI ATTENZIONE**

**E/O IPERATTIVITA'** (ADHD):

Percorsi di Diagnosi e di Cura

Sala Marzio Tremaglia Teatro Donizetti Piazza Cayour, 14 Venerdì 23 Maggio 2014



IL DISTURBO DA DEFICIT DI ATTENZIONE E/O IPERATTIVITA' (ADHD) Percorsi di Diagnosi e di Cura

#### PROGRAMMA

Ore 9,00 Presentazione del Convegno Laura Salvon

Prima parte : Dall'osservazione quotidiana agli approcci diagnostici terapeutici

Ore 9,30 Cos'è il Disturbo da deficit di attenzione e/o iperattività (ADHD): Dalla diagnosi alla cura Stefano Conte

Ore 10,30 Aspetti neuro cognitivi e valutazione neuropsicologica dei bambini con Disturbo da Deficit di attenzione e/o iperattività Gianmarco Marzocchi

Ore 11.15 Pausa

Ore 11,30 La presa in carico del bambino con ADHD : il lavoro con il bambino Paola Effedri

Ore 12,00 La presa in carico del bambino con ADHD : il lavoro con i genitori Valeria Renzetti

Ore 12,30 La presa in carico del bambino con ADHD : il lavoro con gli insegnanti *Gianluca Daffi* 

Ore 13,00-13,30 Dibattite

Pausa Pranzo

#### Ore 14.30

Seconda Parte : L'importanza della coopera-zione tra scuola, famiglia e specialisti

Ore 14.40 Projezione del film documento AIFA "Quando gli aeroplanini sono arancioni.

Ore 15,00 Gli interventi dell'associazione AIFA

Ore 15,30 L'esperienza dello sportello per i genitori Simona Valoti

Ore 16,00 La normativa scolastica relativa all'ADHD Antonella Giannellini

Ore 16.30- 17.30 Discussione e Conclusioni

Per ricevere la newsletter iscriversi al seguente indirizzo: <u>http://crc.marionegri.it/bonati/adhdnews/subscribe.html</u>

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

## 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