



## INDICE:

1. Dalle banche dati bibliografiche	pag. 2
2. Documenti	
<p>Masi G, et al.  <b>EMOTIONAL REACTIVITY IN REFERRED YOUTH WITH DISRUPTIVE BEHAVIOR DISORDERS: THE ROLE OF THE CALLOUS-UNEMOTIONAL TRAITS.</b>            Psychiatry Res. 2014;220:426-32.</p>	pag. 46
<p>Piccini G, et al.  <b>DEVELOPMENTAL LAG OF VISUOSPATIAL ATTENTION IN DUCHENNE MUSCULAR DYSTROPHY.</b>            Res Dev Disabil. 2015;36:55-61.</p>	pag. 53
<p><b>ABSTRACT relativi all'ADHD</b>  <b>XXVI CONGRESSO NAZIONALE SINPIA</b>            Roma, 10-13 settembre 2014.</p>	pag. 60

## **BIBLIOGRAFIA ADHD NOVEMBRE 2014**

Acta Orthop Traumatol Turc. 2014;48:67-72.

### **ASSOCIATION BETWEEN ATTENTION DEFICIT AND HYPERACTIVITY DISORDER AND PERTHES DISEASE.**

**Turkmen I, Poyanli O, Unay K, et al.**

**OBJECTIVE:** The aim of this study was to determine whether or not there is an association between attention deficit and hyperactivity disorder (ADHD) and Perthes disease.

**METHODS:** The study included 3 groups of patients: Perthes patients, trauma patients, and orthopedic patients without Perthes disease or history of trauma. Each group was comprised of 56 males and 4 females. Patients were evaluated for present or past diseases, exposure to second-hand smoke, the age at which they had begun to walk, history of trauma prior to Perthes diagnosis in the Perthes group, weight, height and body mass index (BMI). Eighteen questions on the DSM-4 (Diagnostic and Statistical Manual of Mental Disorders-Fourth Edition) ADHD checklist was used in the psychiatric evaluation of patients. The rate of ADHD was compared between groups.

**RESULTS:** Attention deficit and hyperactivity disorder was diagnosed in 7 patients in the Perthes group, 3 in the trauma group, and 3 in the non-trauma group; and this difference was not significant ( $p=0.160$ ).

**CONCLUSION:** There were no significant differences in the rate of ADHD between trauma and non-trauma groups of Perthes patients, which suggests no association between ADHD and Perthes disease.

Addict Behav. 2014 Apr;39:824-28.

### **REDUCING RISK FOR ILLICIT DRUG USE AND PRESCRIPTION DRUG MISUSE: HIGH SCHOOL GAY-STRAIGHT ALLIANCES AND LESBIAN, GAY, BISEXUAL, AND TRANSGENDER YOUTH.**

**Heck NC, Livingston NA, Flentje A, et al.**

Previous research suggests that lesbian, gay, bisexual, and transgender (LGBT) youth are at elevated risk for using illicit drugs and misusing prescription drugs relative to heterosexual youth. Previous research also indicates that LGBT youth who attend high schools with a gay-straight alliance (GSA) report having fewer alcohol problems and lower levels of cigarette smoking. The present study investigates whether the absence of a GSA is associated with risk for illicit drug use and prescription drug misuse in a sample of 475 LGBT high school students (M age=16.79) who completed an online survey. After controlling for demographic variables and risk factors associated with illicit drug use, the results of 12 logistic regression analyses revealed that LGBT youth attending a high school without a GSA evidenced increased risk for using cocaine (adjusted odds ratio [adjOR]=3.11; 95% confidence interval [95% CI]=1.23-7.86), hallucinogens (adjOR=2.59; 95% CI=1.18-5.70), and marijuana (adjOR=2.22; 95% CI=1.37-3.59) relative to peers attending a high school with a GSA. Youth without a GSA also evidenced increased risk for the misuse of ADHD medication (adjOR=2.00; 95% CI=1.02-3.92) and prescription pain medication (adjOR=2.00; 95% CI=1.10-3.65). These findings extend the research base related to GSAs and further demonstrate the importance of providing LGBT youth with opportunities for socialization and support within the school setting. Important limitations of the present study are reviewed.

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.

**TREATMENT COMPLIANCE OR MEDICATION ADHERENCE IN CHILDREN AND ADOLESCENTS ON ADHD MEDICATION IN CLINICAL PRACTICE: RESULTS FROM THE COMPLY OBSERVATIONAL STUDY.**

**Wehmeier PM, Dittmann RW, Banaschewski T.**

Although the efficacy and tolerability of ADHD medications have been investigated fairly extensively, there are very few data comparing the different types of medication (e.g. psychostimulants, non-stimulants) in terms of medication adherence. The primary research objective of the COMPLY observational study was to evaluate medication adherence (i.e. compliance) over 1 year in children and adolescents with ADHD in a routine clinical setting. COMPLY was a prospective 12-month, observational, open-label study that included children and adolescents, aged 6 to 17 years, with ADHD. Medication adherence (i.e. compliance) was measured using the Pediatric Compliance Self-Rating (PCSR) instrument and using items 1 to 4 of the Medication Adherence Rating Scale (MARS). A total of 504 patients were enrolled. At baseline, 252 patients (50.0 %) were prescribed non-stimulant (atomoxetine) medication and 247 patients (49.0 %) were prescribed psychostimulant medication. Both types of medication were prescribed concomitantly in five patients (1.0 %). After 12 months, 123 patients (48.8 %) were taking atomoxetine and 176 patients (71.3 %) were taking psychostimulants. Adherence (PCSR score (greater-than or equal to 5) was present in both groups (atomoxetine: 67.5 %; psychostimulant: 74.2 %) throughout the observation period. MARS scores declined over time in both groups (atomoxetine: from 3.7 to 2.9; psychostimulant: from 3.6 to 3.1), indicating a deterioration in adherence. There was no statistically significant difference in terms of medication adherence between the two groups.

Am J Psychiatry. 2014 Jul;171:723-28.

**ADHD AND PREGNANCY.**

**Freeman MP.**

Attention deficit hyperactivity disorder (ADHD) has been increasingly recognized and treated in children and adults in recent years. As a result, a growing number of women enter their reproductive years treated with medication for ADHD or are diagnosed and start medication during their reproductive years. A common question in perinatal psychiatry regards the risk-benefit profile of pharmacotherapy for ADHD, particularly with stimulants. At this time, there are no guidelines to inform the treatment of ADHD across pregnancy and the postpartum period. Concerns about in utero exposure to stimulants are based primarily on the impact these medications might have on fetal growth. While stimulants do not appear to be associated with major congenital malformations, more human data regarding potential behavioral teratogenicity are needed in order to understand both the short- and long-term risks. Severity of illness, presence of comorbid disorders, and degree of impairment have an impact on treatment decisions. Crucial considerations include driving safety and ability to function in occupational roles. While most women can successfully avoid the use of stimulant medication during pregnancy, there are cases in which the benefits of stimulant treatment outweigh known and putative risks of in utero medication exposure.

American Journal of Criminal Justice. 2014 Sep;39:411-24.

**FLEDGLING PSYCHOPATHIC FEATURES AND PATHOLOGICAL DELINQUENCY: NEW EVIDENCE.**

**DeLisi M, Dansby T, Peters DJ, et al.**

Fledgling psychopathy is a construct that has proven useful in organizing the nomological network of conduct problems and psychopathology in children and adolescents. Drawing on data from an institutionalized sample of delinquents (n = 252), the current study compared ADHD, CD, and ADHD + CD youth on psychopathic personality features and their association with pathological delinquency. Youths with ADHD + CD were significantly more psychopathic than their peers. Although callousness, unemotionality, and remorselessness are generally theorized to define the fledgling psychopathic youth, ROC-AUC models found that thrillseeking and impulsiveness were the strongest classification variables for delinquency and violent delinquency at the 90th percentiles. Implications for research and practice with antisocial youth are proffered.

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Anadolu Psikiyatr Derg. 2015;16:69-73.

**BIRTH ORDER IN CHILDREN DIAGNOSED WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER.**

**Evrense A, Alparslan S, Yorbik O.**

**Objective:** Etiopathogenesis of attention deficit hyperactivity disorder (ADHD) has not been elucidated. It has been thought that environmental and genetic factors played a role in it. Perinatal fetal traumas might cause minimal brain damage. Being a first born child is a risk factor in term of exposure to birth traumas. There are few studies which focus on the effect of birth order in ADHD. The present study aims to analyze the birth order characteristics of children with ADHD.

**Methods:** The birth orders of children, 16 females and 49 boys with ADHD were determined with Slaternulls Index. Data were compared with the control group.

**Results:** The birth order index of children with ADHD was statistically lower compared to the control group. This results indicate that the firstborn children are more likely to have ADHD.

**Discussion:** The results of this research show first or one of the first born children are more under exposure to perinatal traumas and for those reason minimal brain damages play an important role in etiopatho-genesis of ADHD.

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Ann Epidemiol. 2014 Sep;24:629-34, 634.

**MEDIATORS OF THE ASSOCIATION BETWEEN PARENTAL SEVERE MENTAL ILLNESS AND OFFSPRING NEURODEVELOPMENTAL PROBLEMS.**

**McCoy BM, Rickert ME, Class QA, et al.**

**PURPOSE:** Parental severe mental illness (SMI) is associated with an increased risk of offspring autism spectrum disorder (ASD) and attention deficit hyperactivity disorder (ADHD). We conducted a study to examine the extent to which risk of preterm birth, low birth weight, and small for gestational age mediated this association.

**METHODS:** We obtained data on offspring born 1992-2001 in Sweden (n = 870,017) through the linkage of multiple population-based registers. We used logistic and Cox regression to assess the associations between parental SMI, adverse pregnancy outcomes, and offspring ASD and ADHD, as well as tested whether adverse pregnancy outcomes served as mediators.

**RESULTS:** After controlling for measured covariates, maternal and paternal SMI were associated with an increased risk for preterm birth, low birth weight, and gestational age, and for offspring ASD and ADHD. These pregnancy outcomes were also associated with an increased risk of ASD and ADHD. We found that pregnancy outcomes did not mediate the association between parental SMI and offspring ASD and ADHD, as there was no substantial change in magnitude of the risk estimates after controlling for pregnancy outcomes.

**CONCLUSIONS:** Parental SMI and adverse pregnancy outcomes appear to be independent risk factors for offspring ASD and ADHD.

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Annu Rev Clin Psychol. 2014;10:529-51.

**HOW TO UNDERSTAND DIVERGENT VIEWS ON BIPOLAR DISORDER IN YOUTH.**

**Carlson GA, Klein DN.**

There are two divergent viewpoints on the phenomenology and outcome of bipolar I (BP I) disorder in youth. Disparities evolved as unintended consequences from investigators' inconsistencies both in translating the Diagnostic and Statistical Manual of Mental Disorders (DSM)-III, DSM-III-R, and DSM-IV criteria and in operationalizing them differently in their standardized assessments. Rates of conservatively diagnosed BP I are lower both in community studies of youths than in adults and from liberally defined BP I in youths. Rates of co-occurring attention-deficit hyperactivity disorder (ADHD) are lower in conservatively than liberally defined children and adolescents with BP I. Rates of both BP I and of ADHD are lower in offspring of BP I probands, and outcome more closely approximates that of adults with BP I in conservatively versus liberally defined children

and teens with BP I. Both perspectives can claim evidence for reliability and validity that support their positions. However, the samples are so different that it is difficult to compare studies conducted from these different perspectives.

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Annu Rev Clin Psychol. 2014;10:607-39.

**ATTENTION-DEFICIT/HYPERACTIVITY DISORDER AND RISK OF SUBSTANCE USE DISORDER: DEVELOPMENTAL CONSIDERATIONS, POTENTIAL PATHWAYS, AND OPPORTUNITIES FOR RESEARCH .**

**Molina BS, Pelham WE, Jr.**

Many opportunities to explain attention-deficit/hyperactivity disorder (ADHD)-related risk of substance use disorder (SUD) remain available for study. We detail these opportunities by considering characteristics of children with ADHD and factors affecting their outcomes side by side with overlapping variables in the developmental literature on SUD etiology. Although serious conduct problems are a known contributor to ADHD-related risk of SUD, few studies have considered their emergence developmentally and in relation to other candidate mediators and moderators that could also explain risk and be intervention targets. Common ADHD-related impairments, such as school difficulties, are in need of research. Heterogeneous social impairments have the potential for predisposing, and buffering, influences. Research on neurocognitive domains should move beyond standard executive function batteries to measure deficits in the interface between cognitive control, reward, and motivation. Ultimately, maximizing prediction will depend, as it has in the SUD literature, on simultaneous consideration of multiple risk factors.

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Arch Dis Child. 2014;99:A555.

**PHARMACOLOGIC TREATMENT-PART OF THE THERAPEUTIC PLAN IN ADHD MANAGEMENT.**

**Plesca DA, Houssein TS, Dinu I, et al.**

**Background and aims** Attention deficit hyperactivity disorder (ADHD) is a neurobehavioral disorder generally characterised by inattention, distractibility, impulsivity, hyperactivity. Medication does not cure ADHD, but it is used to control the symptoms. The goal of the study was to determine the impact of pharmacologic treatment on symptoms control in ADHD paediatric patients.

**Methods** The efficacy of pharmacologic treatment was assessed in 82 children patients of 5-12 years old diagnosed with ADHD. 33 patients received treatment with atomoxetine, 26 patients underwent treatment with methylphenidate and 23 patients weren't receiving pharmacological treatment (control group). The ADHD symptoms were screened with parent-rated Child Symptom Inventory-4 (CSI-4) scale at first visit to the doctor and three months after.

**Results** CSI-4 scale scores were statistically analysed. Between-subjects analysis taking as factor the treatment group highlighted a statistical significant difference ( $p < 0.001$ ) between the two time points (baseline and 3 months after) which corresponds to an improvement of the disease symptoms.

**Conclusions** Pharmacologic treatment significantly reduced the ADHD symptoms in children on the basis of parent-rate CSI-4 scoring. Medication doesn't cure, but it has positive impact in the management of ADHD syndrome.

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Arch Dis Child. 2014;99:A204-A205.

#### GLUTEN FREE DIET FOR CHILDREN WITH ATTENTION DEFICIT AND HYPERACTIVITY DISORDER.

**Lykogeorgou M, Karkelis S, Papadaki-Papandreou O, et al.**

**Background and aims** Attention deficit and hyperactivity disorder (ADHD) is a complex neurodevelopmental-neurobiological disorder of behaviour, which is characterised by increased hyperactivity levels. Also, many of the children diagnosed with ADHD have significant nutritional problems. The aim of the study was to investigate the correlation of the hyperactivity status of these children with major nutritional changes using gluten free diet.

**Methods** A total number of 48 children aged 4.5 to 10 years were enrolled. All of them were diagnosed with attention deficit and hyperactivity disorder. Also, all children were tested for IgA deficiency, EMA and anti-tTg autoantibodies, and 3 children with abnormal tests were excluded. The 45 remaining children group was randomly divided in two subgroups: 22 of the children started gluten free diet (group A) and the rest 23 children continued their previous diet (group B). Hyperactivity status was measured using properly arranged questionnaire model and special scoring system for the therapist and the parents. Statistical analysis was performed using the statistical program SPSS/19 and x2-test.

**Results** After 6 months of intervention, statistical significant difference ( $p < 0.001$ ) was found in hyperactivity status between groups A and B, which was maintained also after 12 months.

**Conclusions** Children suffering from attention deficit and hyperactivity disorder have increased hyperactivity status, but it seems that gluten free diet has much to offer in order to lower hyperactivity levels.

Arch Dis Child. 2014;99:A252-A253.

#### ENTORHINAL CORTICAL THINNING AND ADHD AND RELATIONAL PROBLEMS IN VLBW ADOLESCENTS .

**Lozano-Botellero V, Indredavik MS, Skranes J, et al.**

**Background** Children born preterm present higher rates of ADHD symptoms and autistic traits than the general population. Entorhinal cortical abnormalities have been related to cognitive deficits in the preterm population, and to psychiatric and neurodevelopmental disorders in the general population.

**Aim** To assess whether ADHD symptoms and relational problems are associated with changes in entorhinal cortical thickness in very low birth weight (VLBW) adolescents.

**Design/methods** Fifty VLBW (birth weight (less-than or equal to)1500 g) and 57 term control adolescents were assessed at 14-15 years of age with: ADHD Rating Scale IV (mother report), Strengths and Difficulties Questionnaire (SDQ mother report), Child Behaviour Check List (CBCL mother report) and Autism Spectrum Screening Questionnaire (ASSQ). Entorhinal cortical thickness (mm) was obtained using an automated MRI segmentation technique (Freesurfer). Associations were analysed by linear regression, adjusted for age, gender and socioeconomic status, and corrected for multiple comparisons (Benjamini-Hochberg procedure). Results VLBW adolescents had higher ADHD and ASSQ scores than controls. On MRI, they had thinner entorhinal cortex compared to controls. Thinner entorhinal cortex was associated with higher ASSQ scores (Left:  $B = -0.946$  (-1.517 to -0.374),  $p = 0.002$ ; Right:  $B = -0.759$  (-1.308 to -0.210),  $p = 0.008$ ), and higher SDQ Peer Problems Scale scores (Right:  $B = -0.254$  (-0.459 to -0.050),  $p = 0.016$ ).

**Conclusion** Relational problems were associated with entorhinal cortical thinning in adolescents born preterm with VLBW, while associations were not found for ADHD symptoms. The different association in the two symptom groups with the entorhinal cortex might help to identify deviant neural structures and their relation to specific mental disorders.

Arch Dis Child. 2014;99:A517.

#### CONVERGENCE INSUFFICIENCY IN CHILDREN WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER.

**Gomes A, Barbosa A.**

**Background and aims** Near Point of Convergence (NPC) is used to diagnose Convergence Insufficiency (CI), and the existence of common symptoms between CI and Attention Deficit Hyperactivity Disorder (ADHD) has been suggested as an important aspect to be investigated. The aims of this study was to analyse NPC measurement in children with ADHD and the presence of common symptoms between ADHD and CI through



the application of standardised questionnaires and to establish the percentage of individuals that scored questions in common between the ones applied.

**Methods** A transversal study was performed between June and September 2013, with students from 7 to 17 years old, with previous diagnosis of ADHD in which NPC measure was realised and two previously validated questionnaires were applied: one for triage of CI-CISS symptoms and other for the diagnostic criteria to ADHD - MTA-SNP-IV. The data was analysed using SPSS v.20 software.

**Results** Seventy-five students were accepted on the study, 62(82.7%) male and 13 (17.3%) female, with age of 11.24 (plus or minus) 2.33 years old. Mean to NPC was 17.19 cm. NPC was altered in 85.3%. When NPC measure was >5 cm, both questionnaires were positive in 92% of students and 56% of scored questions in common between the two ones.

**Conclusions** This study indicates a high prevalence of CI in the population with ADHD, and shows an overlap of symptoms that were highlighted by comparing the questionnaires applied, suggesting the need to introduce the ocular muscles examination in children with diagnosed or suspected ADHD.

Arch Dis Child. 2014;99:A517.

#### COGNITION IN CHILDREN WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER (ADHD).

**Rusishvili T, Bakhtadze S, Khachapuridze N, et al.**

**Background** Attention deficit hyperactivity disorder (ADHD) is the condition which occurs approximately in 5% of school aged children. The diagnostic tool which will help clinicians to make the precise diagnosis is still absent. Thus child neurologists as well as neuropsychiatrists attempt to seek alternate methods of diagnosis and treatment. The neurophysiologic approaches especially event-related potentials (ERPs) are mostly valuable from this point of view. The later response of ERPs (P3) reflects the most important parts of executive functioning frequently affected in ADHD children-the process of mental effortfulness to select the appropriate behaviour and decision making. Besides the diagnosis the treatment of ADHD is also the point of concern. In recent years EEG biofeedback (Neurofeedback NF) have become the alternative treatment. The aim of our study was assess the changes of EPRs after NF therapy.

**Methods** We have examined 14 patients with ADHDcom without any drug. Age range was 9-12 years. The children were divided into 2 subgroup: the first ADHDcom-1 (6 children) were children with NF treatment and the second subgroup of ADHDcom-2 (8 children) were non treated ones.

**Results** We have found the significant improvement of P3 in ADHD-1 compared with ADHD-2 while NF was non effective for earlier response like N1.

**Conclusions** NF can positively affect on the P3 which is very important in ADHD children as P3 reflects the speed of information processing as well as selection of appropriate action and decision making which are frequently impaired in ADHD children.

Archives of Sexual Behavior. 2014 Nov;43:1525-33.

#### INCREASED GENDER VARIANCE IN AUTISM SPECTRUM DISORDERS AND ATTENTION DEFICIT HYPERACTIVITY DISORDER.

**Strang JF, Kenworthy L, Dominska A, et al.**

Evidence suggests over-representation of autism spectrum disorders (ASDs) and behavioral difficulties among people referred for gender issues, but rates of the wish to be the other gender (gender variance) among different neurodevelopmental disorders are unknown. This chart review study explored rates of gender variance as reported by parents on the Child Behavior Checklist (CBCL) in children with different neurodevelopmental disorders: ASD (N = 147, 24 females and 123 males), attention deficit hyperactivity disorder (ADHD; N = 126, 38 females and 88 males), or a medical neurodevelopmental disorder (N = 116, 57 females and 59 males), were compared with two non-referred groups [control sample (N = 165, 61 females and 104 males) and non-referred participants in the CBCL standardization sample (N = 1,605, 754 females and 851 males)]. Significantly greater proportions of participants with ASD (5.4 %) or ADHD (4.8 %) had parent reported gender variance than in the combined medical group (1.7 %) or non-referred comparison groups (0–0.7 %). As compared to non-referred comparisons, participants with ASD were 7.59 times more likely to express gender variance; participants with

ADHD were 6.64 times more likely to express gender variance. The medical neurodevelopmental disorder group did not differ from non-referred samples in likelihood to express gender variance. Gender variance was related to elevated emotional symptoms in ADHD, but not in ASD. After accounting for sex ratio differences between the neurodevelopmental disorder and non-referred comparison groups, gender variance occurred equally in females and males.

Behav Ther. 2014 Mar;45:177-86.

**THE PREMONITORY URGE TO TIC: MEASUREMENT, CHARACTERISTICS, AND CORRELATES IN OLDER ADOLESCENTS AND ADULTS.**

**Reese HE, Scahill L, Peterson AL, et al.**

In addition to motor and/or vocal tics, many individuals with Tourette syndrome (TS) or chronic tic disorder (CTD) report frequent, uncomfortable sensory phenomena that immediately precede the tics. To date, examination of these premonitory sensations or urges has been limited by inconsistent assessment tools. In this paper, we examine the psychometric properties of a nine-item self-report measure, the Premonitory Urge to Tic Scale (PUTS) and examine the characteristics and correlates of the premonitory urge to tic in a clinical sample of 122 older adolescents and adults with TS or CTD. The PUTS demonstrated adequate internal consistency, temporal stability, and concurrent validity. Premonitory urges were endorsed by the majority of individuals. Most individuals reported some relief from the urges after completing a tic and being able to stop their tics even if only temporarily. Degree of premonitory urges was not significantly correlated with age, and we did not observe any gender differences. Degree of premonitory urges was significantly correlated with estimated IQ and tic severity, but not severity of comorbid obsessive-compulsive disorder or attention-deficit hyperactivity disorder. Also, it was not related to concomitant medication status. These findings represent another step forward in our understanding of the premonitory sensations associated with TS and CTD.

Biometrics. 2014 Mar;70:44-52.

**LIKELIHOOD-BASED ANALYSIS OF LONGITUDINAL DATA FROM OUTCOME-RELATED SAMPLING DESIGNS.**

**Neuhaus JM, Scott AJ, Wild CJ, et al.**

Investigators commonly gather longitudinal data to assess changes in responses over time and to relate these changes to within-subject changes in predictors. With rare or expensive outcomes such as uncommon diseases and costly radiologic measurements, outcome-dependent, and more generally outcome-related, sampling plans can improve estimation efficiency and reduce cost. Longitudinal follow up of subjects gathered in an initial outcome-related sample can then be used to study the trajectories of responses over time and to assess the association of changes in predictors within subjects with change in response. In this article, we develop two likelihood-based approaches for fitting generalized linear mixed models (GLMMs) to longitudinal data from a wide variety of outcome-related sampling designs. The first is an extension of the semi-parametric maximum likelihood approach developed in Neuhaus, Scott and Wild (2002, *Biometrika* 89, 23-37) and Neuhaus, Scott and Wild (2006, *Biometrics* 62, 488-494) and applies quite generally. The second approach is an adaptation of standard conditional likelihood methods and is limited to random intercept models with a canonical link. Data from a study of attention deficit hyperactivity disorder in children motivates the work and illustrates the findings.



BMC Pediatr. 2014;14.

**NEUROFEEDBACK IN CHILDREN WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER (ADHD) - A CONTROLLED MULTICENTER STUDY OF A NON-PHARMACOLOGICAL TREATMENT APPROACH.**

**Holtmann M, Pniewski B, Wachtlin D, et al.**

**Background:** Attention-deficit/hyperactivity disorder (ADHD) is the most common neurobehavioral disorder of childhood and has often a chronic course persisting into adulthood. However, up to 30% of children treated with stimulants either fail to show an improvement or suffer adverse side effects, including decreased appetite, insomnia and irritability and there is no evidence of long term efficacy of stimulants for ADHD. A series of studies has shown that neurofeedback is an effective additional or alternative treatment for children with ADHD, leading to e.g. significant and stable improvement in behavior, attention and IQ. Significant treatment effects of neurofeedback have also been verified in meta-analyses. Most of the trials, however, have been criticized for methodological difficulties, particularly lacking appropriate control conditions and number of patients included. This randomized study examines the efficacy of slow cortical potentials (SCP) -neurofeedback, controlling unspecific effects of the setting by comparing two active treatment modalities.

**Methods/Design:** A total of 144 patients with ADHD, older than six and younger than ten years, in some cases with additional pharmacological treatment, are included in this trial. In five trial centres patients are treated either with SCP-feedback or electromyographic (EMG) -feedback in 25 sessions within 3 months. A comprehensive test battery is conducted before and after treatment and at follow-up 6 month later, to assess core symptoms of ADHD, general psychopathology, attentional performance, comorbid symptoms, intelligence, quality of life and cortical arousal.

**Discussion:** The efficacy of SCP-feedback training for children with ADHD is evaluated in this randomized controlled study. In addition to behavior ratings and psychometric tests neurophysiological parameters serve as dependent variables. Further, the choice of EMG-biofeedback as an active control condition is debated.

**Trials registration:** Current Controlled Trials ISRCTN76187185. Registered 5 February 2009.

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BMC Psychiatry. 2014;14:110.

**EXPLORING STIMULANT TREATMENT IN ADHD: NARRATIVES OF YOUNG ADOLESCENTS AND THEIR PARENTS.**

**Charach A, Yeung E, Volpe T, et al.**

**BACKGROUND:** Young adolescents' and their parents' experiences with Attention-Deficit/Hyperactivity Disorder (ADHD) and its treatment were explored to investigate beliefs and attitudes regarding use of stimulant medication, and their influence on treatment decisions.

**METHODS:** Using in-depth qualitative interviews, 12 adolescents with ADHD aged 12 - 15 years, and their parents described their experiences of ADHD and its treatment. Twenty four interviews, 12 with adolescents and 12 with their parents elicited detailed descriptions of beliefs about ADHD, attitudes about stimulant use and the circumstances surrounding treatment decisions. Verbatim transcripts were iteratively analyzed by a team of researchers following an interpretive interactionist framework.

**RESULTS:** Young people offered three themes describing ADHD: 1) personality trait, 2) physical condition or disorder, and 3) minor issue or concern. Regarding medication use, youth described 1) benefits, 2) changes in sense of self, 3) adverse effects, and 4) desire to discontinue use. Parents' beliefs were more homogeneous than youth beliefs, describing ADHD as a disorder requiring treatment. Most parents noted benefits from stimulant use. Themes were 1) medication as a last resort, 2) allowing the child to reach his or her potential; and 3) concerns about adverse and long-term effects. Families described how responsibility for treatment decisions is transferred from parent to adolescent over time.

**CONCLUSIONS:** Young adolescents can have different beliefs about ADHD and attitudes about medication use from their parents. These beliefs and attitudes influence treatment adherence. Incorporating input from young adolescents when making clinical decisions could potentially improve continuity of treatment for youth with ADHD.

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Brain Cogn. 2014 Apr;86:82-89.

**THE EFFECT OF METHYLPHENIDATE ON VERY LOW FREQUENCY ELECTROENCEPHALOGRAPHY OSCILLATIONS IN ADULT ADHD.**

**Cooper RE, Skirrow C, Tye C, et al.**

Altered very low-frequency electroencephalographic (VLF-EEG) activity is an endophenotype of ADHD in children and adolescents. We investigated VLF-EEG case-control differences in adult samples and the effects of methylphenidate (MPH). A longitudinal case-control study was conducted examining the effects of MPH on VLF-EEG (.02-0.2Hz) during a cued continuous performance task. 41 untreated adults with ADHD and 47 controls were assessed, and 21 cases followed up after MPH treatment, with a similar follow-up for 38 controls (mean follow-up=9.4months). Cases had enhanced frontal and parietal VLF-EEG and increased omission errors. In the whole sample, increased parietal VLF-EEG correlated with increased omission errors. After controlling for subthreshold comorbid symptoms, VLF-EEG case-control differences and treatment effects remained. Post-treatment, a time by group interaction emerged; VLF-EEG and omission errors reduced to the same level as controls, with decreased inattentive symptoms in cases. Reduced VLF-EEG following MPH treatment provides preliminary evidence that changes in VLF-EEG may relate to MPH treatment effects on ADHD symptoms; and that VLF-EEG may be an intermediate phenotype of ADHD. Further studies of the treatment effect of MPH in larger controlled studies are required to formally evaluate any causal link between MPH, VLF-EEG and ADHD symptoms.

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Brain Stimul. 2014;7:760-62.

**LOW FREQUENCY REPETITIVE TRANSCRANIAL MAGNETIC STIMULATION IN CHILDREN WITH ATTENTION DEFICIT/HYPERACTIVITY DISORDER. PRELIMINARY RESULTS.**

**Gomez L, Vidal B, Morales L, et al.**

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Br J Psychiatry. 2014;205:291-97.

**CLINICAL AND SOCIAL FACTORS ASSOCIATED WITH ATTENTION-DEFICIT HYPERACTIVITY DISORDER MEDICATION USE: POPULATION-BASED LONGITUDINAL STUDY.**

**Galera C, Pingault J-B, Michel G, et al.**

**Background:** The impact of longitudinal psychiatric comorbidity, parenting and social characteristics on attention-deficit hyperactivity disorder (ADHD) medication use is still poorly understood.

**Aims:** To assess the baseline and longitudinal influences of behavioural and environmental factors on ADHD medication use.

**Method:** Survival regressions with time-dependent covariates were used to model data from a population-based longitudinal birth cohort. The sample (n = 1920) was assessed from age 5 months to 10 years. Measures of children's psychiatric symptoms, parenting practices and social characteristics available at baseline and during follow-up were used to identify individual and family-level features associated with subsequent use of ADHD medication.

**Results:** Use of ADHD medication ranged from 0.2 to 8.6% between ages 3.5 to 10 years. Hyperactivity-inattention was the strongest predictor of medication use (hazard ratio (HR) = 2.75, 95% CI 2.35-3.22). Among all social variables examined, low maternal education increased the likelihood of medication use (HR = 2.09, 95% CI 1.38-3.18) whereas immigrant status lowered this likelihood (HR = 0.40, 95% CI 0.17-0.92).

**Conclusions:** Beyond ADHD symptoms, the likelihood of receiving ADHD medication is predicted by social variables and not by psychiatric comorbidity or by parenting. This emphasises the need to improve global interventions by offering the same therapeutic opportunities (including medication) as those received by the rest of the population to some subgroups (i.e. immigrants) and by diminishing possible unnecessary prescriptions.

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Can J Psychiatry. 2014 May;59:290.

**EFFECTS OF METHYLPHENIDATE ON ACUTE MATH PERFORMANCE IN CHILDREN WITH ADHD.**

**Jerome L.**

Child Neuropsychol. 2014 Nov;20:677-91.

**The specificity of the Stroop interference score of errors to ADHD in boys.**

**Sørensen L, Plessen KJ, Adolphsottir S, et al.**

The Stroop Interference Test is widely used to assess the inhibition function; however, divergent results have emerged from meta-analyses in children with ADHD. This has led to conflicting results as to whether the Stroop test detects the level of inhibition in these children. We hypothesized that the general approach to include interference scores depending on response time causes conflicting results, whereas recordings of errors may prove a superior measure of the inhibition function in children with ADHD. In the present study, 39 children with an ADHD diagnosis, two subgroups with and without another comorbid mental health disorder, were compared with respect to their interference scores of response time and errors with two subgroups of children with no ADHD. The two subgroups comprised 33 children with another mental health disorder other than ADHD and 56 children with no psychiatric disorder. The between-group analyses detected a multivariate, marginal main effect of an ADHD diagnosis on the Stroop interference scores, and a univariate main effect of an ADHD diagnosis on the interference score of errors. Further, only the interference score of errors predicted significantly the parent reported scores on the Inhibit scale from the Behavior Rating Inventory of Executive Function. These findings support that a Stroop interference score of errors is sensitive for inhibition problems in children with ADHD and encourages the use of Stroop versions including error recordings independent of response time.

Child Neuropsychol. 2014 Nov;20:641-61.

**SMALLER SPLENIUM IN CHILDREN WITH NONVERBAL LEARNING DISABILITY COMPARED TO CONTROLS, HIGH-FUNCTIONING AUTISM AND ADHD.**

**Fine JG, Musielak KA, Semrud-Clikeman M.**

The current study investigated morphological differences in the corpus callosum in children ages 8 to 18 years old with nonverbal learning disability (NLD; n = 19), high-functioning autism (HFA; n = 23), predominantly inattentive ADHD (ADHD:PI; n = 23), and combined type ADHD (ADHD:C; n = 25), as well as those demonstrating typical development (n = 57). Midsagittal area of the corpus callosum and five midsagittal anterior-to-posterior corpus callosum segments were examined using magnetic resonance imaging. Controlling for midsagittal brain area and age, no group differences were found for total corpus callosum area. This finding indicates that higher functioning children on the autistic spectrum do not have smaller corpus callosi as has been found in previous research with heterogeneous samples. Following segmentation of the corpus callosum, the NLD group was observed to have significantly smaller splenia compared to all other groups. Smaller splenia in the NLD group was associated with lower WASI PIQ scores but not WASI VIQ scores. Children with HFA were observed to have larger midbody areas than children with NLD and neurotypically developing children. Children with HFA and NLD demonstrated behavioral symptoms of inattention and hyperactivity similar to the ADHD groups indicating that corpus callosum differences seen in the NLD and HFA groups are not related to these behaviors.

Child Care Health Dev. 2014 Nov;40:775-86.

**ADHD AND TRANSITIONS TO ADULT MENTAL HEALTH SERVICES: A SCOPING REVIEW.**

**Swift KD, Sayal K, Hollis C.**

There is increased awareness that attention deficit hyperactivity disorder (ADHD) continues into adulthood. Thus, health services are faced with a new challenge in providing a 'smooth' transition to adult services appropriate for young people with ADHD. This scoping review sought to identify the literature addressing

transition for young people with ADHD to adult mental health services (AMHS). A scoping review, in which the search terms 'ADHD' and 'Transition' or 'Transfer' were entered into eight healthcare publication databases facilitated by NHS Evidence to identify both published and unpublished papers between 2000 and June 2013. Additional informal searches were also undertaken. Twenty-three papers were selected for this review. This review confirms the lack of research explicitly tracking transition from Paediatrics/Child and Adolescent Mental Health Services (CAMHS) to AMHS for young people with ADHD. Only four papers directly studying transition for ADHD patients were identified. Three further studies surveyed clinician perspectives. Taken together, the studies address a number of issues in relation to transition, including the developmental course of ADHD symptoms, appropriate adult care, knowledge and communication, unmet need, comorbidities, environmental demands and medication cessation/dosage during the transition period. While literature surrounding transition exists, the scope of the evidence showing successful and unsuccessful transition activity from Paediatric and CAMHS to AMHS for young people with ADHD is limited. Future quality research in the form of audits, longitudinal tracking studies and service evaluations are required if we are truly to understand and identify what is needed and currently available for successful transition to an appropriate adult service for ADHD patients.

Child Care Health Dev. 2014 Nov;40:853-62.

**FAMILY ENVIRONMENT AND ATTENTION-DEFICIT/HYPERACTIVITY DISORDER IN ADOPTED CHILDREN: ASSOCIATIONS WITH FAMILY COHESION AND ADAPTABILITY.**

**Crea TM, Chan K, Barth RP.**

**Background** Positive family environments are crucial in promoting children's emotional and behavioural well-being, and may also buffer development of attention-deficit/hyperactivity disorder (ADHD). ADHD is highly heritable, but psychosocial factors in the family environment, particularly family cohesion and communication, may mediate genetic predispositions. The purpose of the current study is to examine the mediating influence of the adoptive family environment between pre-adoptive risk factors and youths' ADHD symptomatology at 14 years post adoption.

**Methods** The data used in this study were obtained from the fourth wave of the California Long-Range Adoption Study (CLAS) (n = 449). Using structural equation modelling (SEM), family sense of coherence and family adaptability were tested as possible mediators between environmental and biological predictors and ADHD symptomatology. Predictors included birthweight, gender, age at adoption, adoption from foster care, transracial adoption status, ethnicity and having a previous diagnosis of ADHD.

**Results** Results show that, while adoption from foster care is negatively associated with family functioning, higher family cohesion and adaptability mediate this influence on children's ADHD symptomatology. Older age of adoption directly predicts greater ADHD symptoms with no mediating influence of the family environment.

**Conclusions** The mediating influence of the family environment between children's risk factors and ADHD symptoms suggests that family intervention strategies may be helpful in improving adopted children's outcomes. Once children are adopted, targeting family communication patterns and dynamics may be an additional part of developing an evidence-based, post-adoption services toolkit.

Clin EEG Neurosci. 2014;45:231-37.

**EEG DIFFERENCES BETWEEN THE COMBINED AND INATTENTIVE TYPES OF ATTENTION-DEFICIT/HYPERACTIVITY DISORDER IN GIRLS: A FURTHER INVESTIGATION.**

**Dupuy FE, Clarke AR, Barry RJ, et al.**

This study further investigated electroencephalogram (EEG) differences between girls with the Combined and Inattentive types of attention-deficit/hyperactivity disorder (AD/HD). We selected subjects with widely separated scores on hyperactivity-impulsivity symptoms to behaviorally exaggerate diagnostic group differences. Twenty girls with AD/HD Combined type, 20 girls with AD/HD Inattentive type, and 20 controls (aged 7-12 years) had an eyes-closed resting EEG recorded from 19 electrodes. The EEG was fast Fourier transformed, and estimates for total power, absolute and relative power in the delta, theta, alpha, and beta frequency bands, and the theta/beta ratio were calculated and analyzed in 9 scalp regions. Girls of the Combined type, compared with girls of the

Inattentive type, had elevated midline total power, elevated temporal absolute alpha activity, elevated posterior absolute beta activity, reduced right hemisphere relative delta and reduced left hemisphere relative alpha activity, and reduced theta/beta ratio in the left hemisphere. Although topographic differences were again found between the AD/HD types, significant global differences remain elusive in the EEGs of girls with the Combined and Inattentive types. Despite creating behaviorally exaggerated AD/HD type groups, girls' EEG activity failed to replicate differences found previously in mixed-sex groups. The EEG profiles of AD/HD types in girls are markedly different from those found in boys. This reinforces the notion that it is no longer appropriate to apply the male-based literature to all AD/HD groups; rather, the use of single-sex subject groups is necessary in EEG research of AD/HD.

Codas. 2013;25:337-41.

#### **VISUAL-MOTOR PERCEPTION IN STUDENTS WITH ATTENTION DEFICIT WITH HYPERACTIVITY DISORDER.**

**Germano GD, Pinheiro FH, Okuda PM, et al.**

**PURPOSE:** The aim of this study was to characterize and to compare the visual-motor perception of students with Attention Deficit with Hyperactivity Disorder (ADHD) with students with good academic performance.

**METHODS:** Forty students from 2nd to 5th grades of an elementary public school, male gender (100%), aged between 7 and 10 years and 8 months old participated, divided into: GI (20 students with ADHD) and GII (20 students with good academic performance), paired according to age, schooling and gender with GI. The students were submitted to Developmental Test of Visual Perception (DTVP-2).

**RESULTS:** The students of GI presented low performance in spatial position and visual closure (reduced motor) and inferior age equivalent in reduced motor perception, when compared to GII.

**CONCLUSION:** The difficulties in visual-motor perception presented by students of GI cannot be attributed to a primary deficit, but to a secondary phenomenon of inattention that interferes directly in their visual-motor performance.

Dev Neuropsychol. 2014;39:249-61.

#### **DIFFERENTIATING BETWEEN COMORBIDITY AND SYMPTOM OVERLAP IN ADHD AND EARLY ONSET BIPOLAR DISORDER.**

**Udal AH, Egeland J, Oygarden B, et al.**

Reported rates of comorbidity between early onset bipolar disorder (BD) and attention deficit hyperactivity disorder (ADHD) have a wide range, perhaps due to developmental issues and differences in interpretation of overlapping symptoms. We compared questionnaire-based and neuropsychological measures of inattention and impulsivity/hyperactivity, in children/adolescents with ADHD combined subtype (ADHD-C; n26), concurrent ADHD-C and BD (n15), BD (n25) with Controls (n69). Sub-analyses were performed on BD with and without inattention symptoms. The two ADHD-C groups displayed neuropsychological impairments that were not found in the BD group in spite of subjective and questionnaire-rated inattention. The findings caution against over-diagnosis of ADHD in BD.

Dev Period Med. 2014 Jul;18:400-04.

#### **INFLUENCE OF SMOKING INTOXICANTS ON DENTAL STATUS. LITERATURE SEARCH AND OWN EXPERIENCE.**

**Hilt A, Rybarczyk-Townsend E.**

Amphetamines are phenylpropane derivatives belonging to the group of psychostimulating substances. Within the space of years, on account of their stimulating properties, they were used as treatment substances, e.g. in Attention deficit hyperactivity disorder (ADHD), in obesity as slimming substances, in preventing of paroxysmal drowsiness, as dilating bronchi substances, used as some dope in sports and willingly abused among drug addicts because of long lasting exciting euphoria after use. Methamphetamine, an amphetamine derivative, has even stronger and longer lasting effect. The study presents characteristics of a popular, among teenagers, addictive substance - amphetamine and its derivative- methamphetamine and its influence on teeth after using it



in a smoking form. The condition of oral cavity of a 17-year-old patient, who has been using methamphetamine in a smoking form for about 3 years, was described. In the oral cavity of the patient numerous and extensive caries lesions were noticed, placed mainly in the labial cervical area of teeth as well as, a considerable damage of teeth's crowns and teeth loss. The patient needed complex dental treatment: conservative, endodontic, surgical and prosthetic. The use of intoxicating substances, derivatives of amphetamine in form of regular smoking caused a considerable damage of tooth tissues, leading to their loss.

Dev Med Child Neurol. 2013;55:13.

#### THE IMPLEMENTATION OF AN INTERNET-BASED SYSTEM FOR MONITORING ATTENTION-DEFICIT HYPERACTIVITY DISORDER IN THE COMMUNITY.

**Parker J, Harpin V, Chalhoub N, et al.**

**Background:** Attention-deficit hyperactivity disorder (ADHD) is a long-term condition which can require long-term service intervention (s) and monitoring from childhood into adult life. However, as a result of an often complex assessment and treatment process and inefficient methods of data collection, little is known regarding long-term ADHD outcomes. Therefore new innovative methods of collecting data are required.

**Participants and Methods:** An on-line multi-media [Health Tracker (HT)] was used to enable children with ADHD as young as five, parents, and teachers to input data through innovative computer-based electronic questionnaires. Eighteen clinicians and more than 70 people with ADHD (plus parents and teachers) used HT in CAMHS and Neurodisability services in Sheffield over an 18 months period.

**Results:** Technological, clinical utility and usability analysis revealed that the utilisation of HT enabled people with ADHD, parents and teachers to provide valuable data that could be interpreted efficiently and effectively by clinicians. Clinicians were also able to self-audit against NICE guidelines. However, technological, clinical utility and usability limitations created specific barriers to use. These included system reliability, computer literacy and access, and clinical time constraints.

**Conclusion:** The collection of electronic data from a community population via an on-line system is a feasible concept and creates the potential to monitor ADHD service users from childhood to adult life. In addition, the utilisation of an on-line system may also create much needed longitudinal cohort data that will allow for a long-term evaluation of service delivery. However, further work is needed to develop the technological capability, clinical utility and usability requirements.

Dev Med Child Neurol. 2014;56:10.

#### GLUTAMATE AND GABA IN YOUNG CHILDREN WITH ADHD: A STRESS ASSOCIATED WITH PARENT1H MRS STUDY AT 7T.

**Mahone EM, Ryan M, Denckla MB, et al.**

**Background:** Maturation of frontal-striatal systems in children occurs during critical developmental periods. This study used high-field H MR spectroscopy (MRS) at 7.0 Tesla to measure concentrations of glutamate (Glu) and GABA, implicated in the neuropathology of ADHD.

**Methods:** Participants included 20 children with ADHD (medication- naive, screened for comorbidities) and 24 controls, ages 5-10 years. Single voxel 1H MRS was performed at 7T using a 32-channel volume head coil. Spectra were acquired in the left hemisphere in the anterior cingulate (ACC), dorsolateral prefrontal cortex (DLPFC), premotor cortex (PMC) and striatum (STR), with voxel volumes of 5-9 mL. Linear mixedeffects models (LME) analyses were used to examine group differences in regional metabolite concentrations, controlling for age and sex.

**Results:** The MRS protocol was well tolerated in all children. Compared to controls, children with ADHD had significantly lower overall GABA/Cr ( $p=0.035$ ), and GABA/Cr in left STR ( $p<0.015$ ). The ADHD group also had 11% higher overall Glu concentrations; however, they also had higher Cr and NAA concentrations, resulting in no group differences in Glu/ Cr or NAA/Cr.

**Discussion:** These data demonstrate feasibility and tolerability of 7T MRS studies in children. The findings are consistent with prior MRS research at 3T, which showed reduced GABA in primary motor and somatosensory



cortices in children with ADHD. The present study (which assessed younger children and both cortical and subcortical gray matter at 7T) revealed greatest differences in striatum, with relative sparing of premotor cortex. High field MRS may provide unique insights into the early neuropathological anomalies in ADHD.

Dev Med Child Neurol. 2014;56:4.

#### **ADHD: THE FINAL COMMON PATHWAY?**

**Anderson V.**

ADHD is a common developmental disorder, characterised by inattention, hyperactivity and impulsivity, and causing significant functional difficulties, including behavioural and social problems, as well as poor educational achievement. While some children demonstrate 'pure' ADHD a large proportion exhibit a range of co-morbidities, including learning problems, speech and language difficulties, social communication problems and conduct disorder. ADHD symptoms are also common in children with a history of brain insult, highlighting the multiple potential pathways to the disorder. The majority of studies addressing ADHD have used clinic-derived samples, where it might be expected that symptoms are more severe and co-morbidities more likely. This presentation will describe preliminary findings from a recently-conducted large-scale, community based study of ADHD, the Children's Attention Project (CAP). The study recruited 6 year-old children, with and without symptoms of ADHD, and followed them up over 18 months, and collected data on a range of outcomes including behaviour profiles, co-morbidities, neuropsychological function and educational achievement. This paper will discuss findings from the CAP study, and compare them to results from other conditions with high risk of ADHD symptoms (e.g., acquired brain injury), in order to better understand the psychological precursors to ADHD.

Encephale. 2013.

#### **PSYCHIATRIC COMORBIDITY RELATED TO CHILDREN WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER AT SCHOOLS IN SFAX, TUNISIA.**

**Khemakhem K, Ayedi H, Moalla Y, et al.**

**Introduction:** Attention deficit hyperactivity disorder (ADHD) is a prevalent behavioral disorder particularly noticed among school children. It is often associated with other psychological troubles at the origin of an additional difficulty that has to be overcome.

**Objective:** Our research's aim was to study the comorbidity of school-aged children diagnosed with ADHD in Sfax, Tunisia.

**Subjects and methods:** A cross-sectional descriptive study was carried out from 1st April 2008 to 1st October 2008. Five hundred and thirteen pupils aged between 6 and 12, from primary arbitrarily chosen schools from Sfax were subjected to this study.

**Measurements were carried out in two steps:** parents and teachers of each child filled in separately Conners questionnaire, then children with a score in subscales inattention, hyperactivity impulsivity higher than 70 were selected for psychiatric interview that was intended to confirm or to invalidate the ADHD diagnosis and the possible comorbid diagnosis. The diagnoses were made according to DSM-IV-TR.

**Results:** We have noticed that 109 pupils exhibited at least one pathological score on the Conners questionnaire. After interviewing these 109 pupils, the results have shown that 51 among them fulfilled criteria of ADHD. Prevalence of ADHD was found to be 9.94 %. About 72.54 % of children with ADHD had one or more comorbid disorder: learning disabilities (23.52 % of cases), anxiety disorder (31.37 % of cases), oppositional defiant disorder in (15.68 % of cases), mood disorder (3.92 % of cases), enuresis (13.72 % of cases) and slight mental retardation (1.95 % of cases).

**Conclusion:** We can say that this study has shown that ADHD school children's psychiatric comorbidity is similar to any other previous study.

Eur Child Adolesc Psychiatry. 2014 Jul;23:519-29.

**NUTRITION, IMMUNOLOGICAL MECHANISMS AND DIETARY IMMUNOMODULATION IN ADHD.**

**Verlaet AA, Noriega DB, Hermans N, et al.**

Attention-deficit hyperactivity disorder (ADHD) etiology is not completely understood, but common comorbid dysfunction of the gastrointestinal and immune system suggests that these systems may be affected by a common genetic background and molecular mechanisms. For example, increased levels of specific cytokines were observed in ADHD. Moreover, ADHD has a high comorbidity with both Th1- and Th2-mediated disorders like ear infections, eczema and asthma. A common pathophysiological mechanism was suggested to underlie both asthma and ADHD, while several genes that are linked to ADHD have immune functions. Furthermore, immunological recognition of food provoking ADHD-like behavior was suggested. An immune imbalance, probably requiring a predisposing genetic background, is therefore suggested to contribute to ADHD etiology, with immune dysregulation being more likely than a single subcellular defect. However, next to allergic mechanisms, also pharmacological mechanisms (especially in case of food additives) might be involved. In addition, though cellular (cytokine-related) rather than antibody-mediated immune mechanisms seem involved, specific immune-inflammatory markers other than antibodies have not been systematically studied in ADHD. Substantial alterations implicated in ADHD apparently occur in the immune system and epigenetic regulation of gene expression. As a result, chronic inflammation and oxidative stress could develop, which can lead to ADHD symptoms, for example by chronic T-cell-mediated neuroinflammation. If immune pathways contribute to ADHD, both its diagnosis and treatment should be reconsidered. Modulation of immune system activity might have potential in ADHD treatment, for example by nutritional approaches providing safe and low-cost ADHD therapy, but further research in these fields is implicated.

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Eur Child Adolesc Psychiatry. 2014.

**EEG THETA AND BETA POWER SPECTRA IN ADOLESCENTS WITH ADHD VERSUS ADOLESCENTS WITH ASD + ADHD.**

**Bink M, Van Boxtel GJM, Popma A, et al.**

Attention problems are common in youngsters with attention deficit hyperactivity disorder (ADHD) as well as in adolescents with combined autism spectrum disorder (ASD) and ADHD. However, it is unknown whether there is psychophysiological overlap and/or a difference in electroencephalogram (EEG) power spectra between ADHD and comorbid ASD and ADHD (ASD + ADHD), on and off stimulant medication. To explore potential differences and overlap, measures of theta and beta power in adolescents diagnosed with ADHD (n = 33) versus adolescents with combined ASD + ADHD (n = 20), categorized by stimulant medication use (57 % of the total sample), were compared. EEG measures were acquired in three conditions: (1) resting state, eyes closed (2) resting state, eyes open and (3) during an oddball task. In addition, performance on the d2 attention test was analyzed. Adolescents with ADHD displayed more absolute theta activity than adolescents with ASD + ADHD during the eyes open and task conditions, independent of stimulant medication use. In addition, only the adolescents with ADHD showed an association between diminished attention test performance and increased theta in the eyes open condition. Results of the current study suggest that although there is behavioral overlap between ADHD characteristics in adolescents with ADHD and adolescents with combined ASD + ADHD, the underlying psychophysiological mechanisms may be different. Adolescents with ASD + ADHD exhibited fewer of the EEG physiological signs usually associated with ADHD, although there was an overlap in attentional problems between the groups. This may indicate that treatments developed for ADHD work differently in some adolescents with ASD + ADHD and adolescents with ADHD only.

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European Journal of Developmental Psychology. 2014 Nov;11:687-700.

**CORRESPONDENCE BETWEEN CHILDREN'S AND ADULTS' RATINGS OF STIMULANT-INDUCED CHANGES IN ADHD BEHAVIOURS IN A CROSSOVER TRIAL WITH MEDICATION-NAIVE CHILDREN.**

**Ramtvedt BE, Sandvik L, Sundet K.**

Correspondence between children's and adults' ratings of changes in ADHD behaviours was investigated in a paediatric ADHD stimulant crossover trial. Thirty-one children completed an ADHD self-report scale each week,

and comparisons were made with an ADHD questionnaire completed by adults (combined parent and teacher ratings). Children's and adults' ratings demonstrated good internal consistency, were significantly associated with the assessment of ADHD behaviours in the placebo condition and showed comparable responsiveness to stimulants at the group level. Furthermore, a large and significant correlation was detected between the two sets of informants' ratings of changes from placebo to both methylphenidate and dextroamphetamine high-dosage conditions, but not from placebo to low-dosage conditions. Agreement in the categorization of best stimulant condition for individual children was significant, but modest from a clinical perspective. The results indicate that children's ratings correspond adequately with adults' ratings, and thus appear to be a complementary outcome measure.

European Journal of Psychology of Education. 2014 Sep;29:467-82.

**SYMPTOMS OF ATTENTION-DEFICIT HYPERACTIVITY DISORDER (ADHD) AND HOME LEARNING ENVIRONMENT (HLE): FINDINGS FROM A LONGITUDINAL STUDY .**

**Schmiedeler S, Niklas F, Schneider W.**

The concept of "Home Learning Environment" (HLE) covers activities in a family providing intellectual stimulation for a child, such as reading to him or her or visiting libraries. Numerous studies have shown an association between HLE and children's cognitive development. In this longitudinal study, we focus on HLE as a predictor for children's behavioral development, namely, for later symptoms of attention-deficit hyperactivity disorder (ADHD), controlling for relevant aspects like socioeconomic status (SES), or television viewing behavior. We analyzed the development of ADHD symptoms from kindergarten to the end of grade 2 and possible associations with HLE, SES, and television exposure, using a German community sample (N = 924). Results indicated that ADHD symptoms were negatively and significantly correlated to HLE for all five measurement points as well as to SES (except T4) and to television exposure for T1 to T4. Observing later development, only early HLE but not SES or television exposure served as a significant predictor for ADHD symptoms at school, when age, sex, and ADHD symptoms in kindergarten were controlled for. A structural equation model showed that HLE acted as a mediator between SES and later ADHD symptoms. Our results highlight the importance of the concept of home learning environment also for children's behavioral development. As a consequence, parents should be supported in offering their children a more favorable learning environment.

Exp Dermatol. 2014;23:e4.

**IMPAIRED INTRACELLULAR GRANULE BIOLOGY: BASIS OF UPREGULATED VIGILANCE MECHANISMS IN CHILDREN WITH ATOPIC DERMATITIS (AD) AND/OR ATTENTION DEFICIT HYPERACTIVITY DISORDER (ADHD).**

**Wolfer W, Krauel K, Bonnekoh B, et al.**

Skin, adjacent mucosa and brain are linked by ectodermal origin and function: surveillance of the environment for potential harm and for survival support. Increased skin vigilance is a hallmark of patients with AD/atopy syndrome. This is based in part on reduction of intracellular storage organelles and disturbed granule release mechanisms in several cell systems resulting in an often adequate but not sustained reaction to stimulation.

**Hypothesis:** Since the functional state of sensory organs is not independent of each other, CNS-reactions requiring sustained granule release (from neurons) may be impaired in AD-patients as well. Likewise, ADHD-patients unable to keep up an enduring CNSresponse might also show altered peripheral granule biology. 11 children with AD (8 m, 3f), 14 matched ADHD-inpatients with confirmed diagnosis (13 m, 1f), and 8 healthy control individuals (HC) without any atopic or psychiatric background (6 m, 2f) were studied in 3 modules: A) child psychiatry, B) dermato-allergology, C) laboratory. In A, using a neuropsychological computer-based test battery [Psytest 2.2, Herzogenrath, Germany], short term (120 signals / 4 min, 'sprint') and long term (900 signals / 30 min, 'endurance') attentiveness towards visual and acoustic stimuli was tested. ADHD symptoms, emotional and behavioural difficulties as well as personality traits (e.g. novelty seeking) were assessed via questionnaires (CBCL, DISYPS II-ADHD, JTCI). In B, the Erlanger Atopie Score (EAS), SCORAD and a prick test with common aero allergens were performed. In C, total serum IgE, eosinophilic cationic protein (ECP) and differential blood count were determined. After stimulation with ionomycin/PMA, granule release velocity of

perforin-containing granules from cytotoxic T lymphocytes (CTL) and of CD63<sup>pos</sup> secretory lysosomes from basophils was quantified by flow cytometry.

**Module A:** 2/11 AD-patients were eliminated from analysis because parents reported a significant number of ADHD symptoms. In the 4 min.- test, AD-children reacted similar to the ADHD-group: significantly slower with more mistakes than HC. In the 30 min.- test, AD-children showed prolonged reaction times as well and slowed down even more over time as compared to HC, but did not make as many errors as ADHD-patients.

**Module B:** 12/14 ADHD-children did not have any AD-symptoms nor any history of AD/atopy. (2/14: rhinoconjunctivitis, positive: skin prick test and family history). ADHD-children showed a white dermographism (13/14) and an EAS of 93 (atopic skin diathesis unclear). 5/11 AD-patients had exacerbated disease (SCORAD > 10, mean EAS 123).

**Module C:** Both, ADHD- and AD-children had elevated (i) IgE levels (7/14, 500 420 kU/l and 5/9, 653 950 kU/l), (ii) eosinophils (9/14, 8.79% and 7/9, 7.76%) and (iii) ECP (8/14, 3130 and 7/9, 3933). In AD- and ADHD-children, perforin<sup>pos</sup> CTL were significantly reduced (1510% and 126%) as compared to HC (219%,  $P < 0.05$ ). After stimulation with ionomycin/PMA, AD- and ADHD-patients released cytotoxic granules, and upregulated CD63 on the cell surface of basophils, faster and more complete as compared to HC ( $P < 0.05$ ). Thus, AD/atopy may be interpreted as a consequence of an increased vigilance of skin, immune and nervous system. Reduction and quick release of storage organelles impair sustainability of stimulus induced reactions. Altered granule transport mechanisms in ADHD are first reported here opening a new way to look at ADHD-pathophysiology. Our work may help to understand why atopy is an independent risk factor for ADHD.

Expert Rev Neurother. 2014 Mar;14:287-99.

#### **SLEEP PROBLEMS AND THEIR EFFECT IN ADHD.**

**Kirov R, Brand S.**

Sleep problems are common in attention-deficit/hyperactivity disorder (ADHD) to the extent that they mimic or exacerbate daytime symptoms expression. In this review, we advocate the need for a better understanding of sleep alterations in youths with ADHD and their impact on neurobehavioral functions including learning, memory and emotional regulation. An in-depth exploration of existing data showed that although extensively studied, the actual nature of sleep problems in ADHD and their effects on daytime behavior are still less well understood. Important issues, among which developmental changes in sleep architecture and role of subtle sleep electroencephalogram signatures, are generally neglected. Future research of sleep effects on behavior in ADHD would benefit from considering developmental aspects and links between brain activation patterns during sleep and wake.

Int J Audiol. 2014 Mar;53:145-52.

#### **EFFECTS OF NOISE AND AUDIOVISUAL CUES ON SPEECH PROCESSING IN ADULTS WITH AND WITHOUT ADHD.**

**Michalek AM, Watson SM, Ash I, et al.**

**OBJECTIVE:** This study examined the interplay among internal (e.g. attention, working memory abilities) and external (e.g. background noise, visual information) factors in individuals with and without ADHD.

**DESIGN:** A 2 x 2 x 6 mixed design with correlational analyses was used to compare participant results on a standardized listening in noise sentence repetition task (QuickSin; Killion et al, 2004 ), presented in an auditory and an audiovisual condition as signal-to-noise ratio (SNR) varied from 25-0 dB and to determine individual differences in working memory capacity and short-term recall.

**STUDY SAMPLE:** Thirty-eight young adults without ADHD and twenty-five young adults with ADHD.

**RESULTS:** Diagnosis, modality, and signal-to-noise ratio all affected the ability to process speech in noise. The interaction between the diagnosis of ADHD, the presence of visual cues, and the level of noise had an effect on a person's ability to process speech in noise.

**CONCLUSION:** Young adults with ADHD benefited less from visual information during noise than young adults without ADHD, an effect influenced by working memory abilities.

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Int J Psychiatry Med. 2014;47:55-63.

**RELATIONSHIP BETWEEN EXTREMITY FRACTURES AND ATTENTION-DEFICIT/HYPERACTIVITY DISORDER SYMPTOMATOLOGY IN ADULTS.**

**Komurcu E, Bilgic A, Herguner S.**

**OBJECTIVE:** Recent studies showed that attention deficit hyperactivity disorder (ADHD) is a lifelong disorder which may be seen in adults as well as children. However, information about the relationship between ADHD and general medical conditions in adulthood is limited. This case-control study aims to determine whether ADHD symptoms are associated with extremity fractures and their clinical characteristics.

**METHODS:** Forty patients (25 male and 15 female; aged 18-50 years) who were seen due to extremity fractures and 40 control subjects were enrolled. Childhood and present ADHD symptoms of the participants were assessed using Wender Utah Rating Scale (WURS) and Adult ADHD Self-Report Scale (ASRS), respectively. Trauma type, reason of the trauma, fracture localization, hospitalization requirement, treatment type, and history of previous fracture(s) of the patients were recorded.

**RESULTS:** Total score and all subscale scores of WURS were higher in the fracture groups compared with controls. Patients also had higher ASRS total score and ASRS hyperactivity-impulsivity subscore than the controls did. WURS irritability, inattentiveness, and behavioral problems/impulsiveness subscore and total score were positively correlated with the history of previous fracture. The patients in whom the reason for the fracture was fighting were also showed higher WURS irritability subscore.

**CONCLUSIONS:** Our results suggest that extremity fractures are associated with ADHD symptoms in adults. These findings may provide an insight into better understanding the lifelong negative impact of ADHD on the physical health of its sufferer.

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Int J Psychiatry Med. 2014;47:41-53.

**SELF-ESTEEM AND PSYCHIATRIC FEATURES OF TURKISH ADOLESCENTS WITH PSYCHOGENIC NON-EPILEPTIC SEIZURES: A COMPARATIVE STUDY WITH EPILEPSY AND HEALTHY CONTROL GROUPS.**

**Say GN, Tasdemir HA, Akbas S, et al.**

**OBJECTIVE:** Children and adolescents with psychogenic non-epileptic seizures (PNES) and epilepsy are known to have psychosocial problems. The aim of the present study was to compare the psychosocial difficulties, history of stressful life events/abuse, psychiatric diagnosis, and self-esteem of adolescents with PNES to the ones with epilepsy and healthy controls at a tertiary care center in Turkey.

**METHOD:** Thirty-four adolescents with PNES diagnosed by video-EEG were compared with 23 adolescents that have epilepsy and 35 healthy volunteers. Comorbid psychiatric diagnoses of participants were examined by semi-structured interviews using Schedule for Affective Disorders and Schizophrenia for School Age Children-Present and Lifetime Version (KSADS-PL). Self-esteem of adolescents was evaluated by Rosenberg Self Esteem Scale (RSES).

**RESULTS:** No differences in sociodemographic features were observed between the groups. The PNES group showed significantly higher rates of parental conflicts, difficulties in relationship with siblings/peers, school underachievement, and history of stressful events/abuse. The rates of comorbid psychiatric disorders were 64.7% in PNES and 47.8% in epilepsy group. The most common disorders in both groups were attention deficit hyperactivity disorder (ADHD) and depressive disorder. The rate of posttraumatic stress disorder (PTSD) was significantly increased in the PNES group. Additionally, adolescents with PNES displayed significantly lower levels of self-esteem than the other groups.

**CONCLUSION:** It could be concluded that both disorders involved a high risk for developing psychiatric disorders; additionally, adolescents with PNES have higher rates of stressors and lower levels of self-esteem.



Findings from this investigation point to the importance of psychiatric interventions in pediatric PNES and also epilepsy.

Int J Clin Pract. 2014;68:1152-60.

**PREDICTORS OF PHARMACOLOGICAL TREATMENT OUTCOMES WITH ATOMOXETINE OR METHYLPHENIDATE IN PATIENTS WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER FROM CHINA, EGYPT, LEBANON, RUSSIAN FEDERATION, TAIWAN, AND UNITED ARAB EMIRATES.**

**Treuer T, Feng Q, Desai D, et al.**

**Background:** The reduced availability of data from non-Western countries limits our ability to understand attention-deficit/hyperactivity disorder (ADHD) treatment outcomes, specifically, adherence and persistence of ADHD in children and adolescents. This analysis assessed predictors of treatment outcomes in a non-Western cohort of patients with ADHD treated with atomoxetine or methylphenidate

**Methods:** Data from a 12-month, prospective, observational study in outpatients aged 6-17 years treated with atomoxetine (N = 234) or methylphenidate (N = 221) were analysed post hoc to determine potential predictors of treatment outcomes. Participating countries included the Russian Federation, China, Taiwan, Egypt, United Arab Emirates and Lebanon. Factors associated with remission were analysed with stepwise multiple logistic regression and classification and regression trees (CART). Cox proportional hazards models with propensity score adjustment assessed differences in atomoxetine persistence among initial-dose cohorts

**Results:** In patients treated with atomoxetine who had available dosing information (N = 134), Cox proportional hazards revealed lower (< 0.5 mg/kg) initial dose was significantly associated with shorter medication persistence ( $p < 0.01$ ). Multiple logistic regression analysis revealed greater rates of remission for atomoxetine-treated patients were associated with age (older), country (United Arab Emirates) and gender (female) (all  $p < 0.05$ ). CART analysis confirmed older age and lack of specific phobias were associated with greater remission rates. For methylphenidate, greater baseline weight (highly correlated with the age factor found for atomoxetine) and prior atomoxetine use were associated with greater remission rates

**Conclusions:** These findings may help clinicians assess factors upon initiation of ADHD treatment to improve course prediction, proper dosing and treatment adherence and persistence.

Int J Psychiatry Clin Pract. 2014;18:272-79.

**ATTENTION DEFICIT HYPERACTIVITY DISORDER IN CHILDREN IS FOUND TO BE RELATED TO THE OCCURRENCE OF ADHD IN SIBLINGS AND THE MALE GENDER, BUT NOT TO BIRTH ORDER, WHEN COMPARED TO HEALTHY CONTROLS.**

**Keshavarzi Z, Bajoghli H, Mohamadi MR, et al.**

**Objective.** The aim of the present study was to explore the extent to which the prevalence of attention deficit hyperactivity disorder (ADHD) in childhood is associated with birth order and gender, and the prevalence of ADHD and mental retardation (MR) in siblings, as compared to healthy controls

**Methods.** Data from 200 children diagnosed with ADHD (mean age: 11.13 years; 10.5% females) were compared to data from 200 healthy controls (mean age: 11.0 years; 27.5% females). The data were related to symptoms of ADHD, birth order, gender, family size, and the occurrence of ADHD and MR in siblings

**Results.** Compared to controls, the occurrence of ADHD was found to be related to the male gender and to the occurrence of ADHD-related symptoms in siblings (odds ratio: 13.50). Birth order and MR were not associated with the occurrence of ADHD and ADHD-related symptoms. ADHD-related symptoms increased if a further sibling also suffered from ADHD

**Conclusions.** Among a sample of Iranian children suffering from ADHD, the ADHD and ADHD-related symptoms in childhood were found to be related to the male gender and to the occurrence of ADHD in siblings. Moreover, birth order was found to be unrelated. The fact that symptoms of ADHD-related symptoms increased if a further sibling was suffering from ADHD, and decreased if a further sibling was suffering from MR, is intriguing and needs further explanation.



Isr Med Assoc J. 2014;16:568-73.

**THE ISRAEL SURVEY OF MENTAL HEALTH AMONG ADOLESCENTS: PREVALENCE OF ATTENTION-DEFICIT/HYPERACTIVITY DISORDER, COMORBIDITY, METHYLPHENIDATE USE, AND HELP-SEEKING PATTERNS.**

**Farbstein I, Mansbach-Kleinfeld I, Auerbach JG, et al.**

**Background:** The prevalence of ADHD is controversial, with many feeling that this disorder is over- or under-diagnosed

**Objectives:** To study the prevalence of attention-deficit/ hyperactivity disorder (ADHD) and its association with sociodemographic characteristics, comorbid mental disorders, medical services, and methylphenidate use in the Israeli adolescent population

**Methods:** The Israel Survey of Mental Health among Adolescents was conducted in a representative national sample of 14null17 year olds and their mothers. The Development and Well-Being Assessment was administered to identify DSM-IV diagnoses of ADHD and comorbid mental and learning disorders, and the results were verified by senior child psychiatrists. Respondents were also asked about their use of medical services and psychotropic drug intake in the past 12 months

**Results:** Three percent of the adolescents met the DSM-IV criteria for ADHD. ADHD was significantly associated with gender (higher prevalence in boys than girls), ethnicity (higher prevalence in Jews than Arabs/Druze), referral to a medical professional, and maternal help-seeking for the emotional or behavioral problems of the adolescent. Medication was prescribed to 2.9% of adolescents: 34.6% with a diagnosis of ADHD had not been prescribed methylphenidate in the past year, and 34.6% of the medicated subjects did not have a diagnosis of ADHD. None of the Arab/Druze adolescents was receiving stimulants compared to 3.7% of the Jewish adolescents

**Conclusions:** Despite advances in public awareness of mental disorders in youth, a substantial proportion of older Israeli adolescents, especially from minority groups, are under-diagnosed or untreated. At the

same time, many, especially from the Jewish majority, are over-diagnosed and potentially over-treated. Ethnic disparities in rates of mental health care highlight the urgent need to identify and overcome barriers to the recognition and treatment of these conditions.

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J AAPOS. 2014 Feb;18:31-35.

**THE LONG-TERM OUTCOMES OF OCULAR TICS IN A PEDIATRIC NEURO-OPHTHALMOLOGY PRACTICE.**

**Bisker ER, McClelland CM, Brown LW, et al.**

**PURPOSE:** To describe the outcome and comorbidities of ocular tics in children evaluated by a pediatric neuro-ophthalmologist.

**METHODS:** The medical records of all consecutive patients in a pediatric neuro-ophthalmology practice diagnosed with ocular tics (eye rolling, blinking, and widening) were retrospectively reviewed. Children with known secondary causes for tics were excluded. Patients, parents, and/or guardians were contacted by telephone to obtain follow-up information.

**RESULTS:** A total of 43 patients were included in the retrospective cohort, with a mean age of 7.8 +/- 4.8 years at diagnosis. Thirty-two patients participated in the follow-up survey, with an average follow-up of 6.1 +/- 3.9 years. None of the 43 children carried a diagnosis of Tourette syndrome or obsessive-compulsive disorder (OCD) at presentation; 1 child had attention deficit hyperactivity disorder (ADHD). At follow-up, 14 of the 32 children (44%) had persistent ocular tics, 3 (9%) reported new nonocular motor tics, 5 (16%) reported new vocal tics, and 4 (13%) developed both nonocular motor and vocal tics. One patient (3%) was formally diagnosed with Tourette syndrome during the follow-up interval, and 3 (9%) were diagnosed with ADHD.

**CONCLUSIONS:** Almost half of the children with ocular tics at presentation had persistent ocular tics on follow-up. New nonocular motor and vocal tics occurred in several patients.

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J Addict Nurs. 2013 Apr;24:108-15.

**THE USE OF THE ADHD SELF-RATING SCALE (ASRS-6) IN THE HOMELESS: PSYCHOMETRIC PROPERTIES, ALCOHOL USE, AND SELF-NURSE AGREEMENT.**

**Hesse M, Thiesen H.**

**BACKGROUND:** Attention deficit/hyperactivity disorder (ADHD) is prevalent in homeless populations, but no studies have assessed the psychometric properties of assessment instruments for this population.

**METHODS:** Self-other agreement on the ADHD Self-Rating Scale 6 was studied using a cohort of admissions to an outreach clinic for the homeless (n = 72). Alcohol use was assessed with the fast alcohol screening test. Other drug use was assessed by interview.

**RESULTS:** For the six-item ASRS-6, the self-nurse correlation was .63 ( $p < .001$ ). Discriminant correlations were low. Higher ASRS-6 scores as rated by both nurse and self-report were associated with illicit drug use but not alcohol problems. Concordance was lower at higher levels of alcohol problems ( $p < .05$ ).

**CONCLUSION:** The observations of experienced nurses converge well with self-reported symptoms of ADHD. Further research is needed to assess the relative contribution of clinical observation and self-report in assessing homeless patients.

J Clin Exp Neuropsychol. 2014 Apr;36:244-60.

**NONWORD READING AND STROOP INTERFERENCE: WHAT DIFFERENTIATES ATTENTION-DEFICIT/HYPERACTIVITY DISORDER AND READING DISABILITY?**

**Stubenrauch C, Freund J, Alecu de FS, et al.**

**BACKGROUND:** Attention deficits and impaired reading performance co-occur more often than expected by chance; however, the underlying mechanism of this association still remains rather unexplored.

**METHOD:** In two consecutive studies, children aged 8 to 12 years with attention-deficit/hyperactivity disorder (ADHD) and children with reading disability (RD) were examined using a 2 (ADHD versus no ADHD) x 2 (RD versus no RD) factorial design. To further delineate deficient interference control from reading processes, we used a newly developed self-paced word/nonword reading task (Experiment 1, n = 68) and a modified computerized Stroop paradigm, including an orthographic phonological neighbor (OPN) condition (Experiment 2, n = 84).

**RESULTS:** RD (compared to non-RD groups) was associated with impairments in both word and nonword reading, while children with ADHD also showed impaired nonword reading. In the Stroop task, RD, but not ADHD, had a significant impact on task performance. Interestingly, a significant interaction between ADHD, RD, and task condition emerged, which was due to particularly slower reaction times to nonwords in children with RD only, while task performance in children with comorbid ADHD and RD resembled that of ADHD only.

**CONCLUSIONS:** Thus, our results demonstrate that impairments in nonword reading were not specific to RD but were also present in children with ADHD. In addition, RD and not ADHD was characterized by poor interference control in the Stroop task. These findings question whether unique cognitive deficits are specific to either ADHD or RD.

J Clin Psychiatry. 2014 May;75:528-29.

**AGE IN SCHOOL COHORT, BORDERLINE PERSONALITY DISORDER, AND NEUROFEEDBACK.**

**Wagner KD.**

J Clin Res Pediatr Endocrinol. 2013;5:229-35.

**PSYCHIATRIC APPROACHES FOR DISORDERS OF SEX DEVELOPMENT: EXPERIENCE OF A MULTIDISCIPLINARY TEAM.**

**Ozbaran B, Ozen S, Goksen D, et al.**

**OBJECTIVE:** Disorders of sex development (DSD) are a group of congenital medical conditions that affect life as a whole. In this study, we aimed to reflect the experience of a multidisciplinary team in the clinical/psychiatric follow-up of a group of children and adolescents with DSD.

**METHODS:** The study group consisted of 51 patients diagnosed with DSD. The Kiddie-Schedule for Affective Disorders and Schizophrenia, Wechsler Intelligence Scale for Children-Revised, Draw a Person Test and Children's Apperception Test, and the Clinical Global Impression Scale (CGIS) were used for psychiatric evaluations.

**RESULTS:** The mean age of the patients was 7.8 years (median: 7.8; min: 1.0; max: 18.0). Genetic evaluation showed 46,XX configuration in 15 patients (29.4%) and 46,XY in 35 (68.6%). One patient (2.0%) was diagnosed to have a sex chromosome disorder. Forty patients (78.4%) had no problems with their given gender identity and gender role. Thirty-four (66.7%) patients had normal intellectual capacity. Twenty-eight (54.9%) patients did not have any psychiatric problem. Depression, anxiety disorders, attention deficit/hyperactivity disorder, and adjustment disorders were the common diagnoses. The mean score of symptom severity on CGIS-severity-baseline was 6.15+/-0.68 and after one year, it was 1.46+/-0.51 ( $Z=-3.236$   $p=0.001$ ). The mean score of CGI-Improvement was 1.23+/-0.44.

**CONCLUSION:** It is important to identify and treat the psychiatric disorders encountered in patients with DSD. A psychiatrist needs to be included in the professional team following these patients. Examination and observation results need to be shared by holding periodic team meetings to establish a wholesome point of view for every unique child.

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J Pediatr. 2014 Jun;164:1333-38.

**EFFECTS OF PRENATAL METHAMPHETAMINE EXPOSURE ON BEHAVIORAL AND COGNITIVE FINDINGS AT 7.5 YEARS OF AGE.**

**Diaz SD, Smith LM, LaGasse LL, et al.**

**OBJECTIVE:** To examine child behavioral and cognitive outcomes after prenatal exposure to methamphetamine.

**STUDY DESIGN:** We enrolled 412 mother-infant pairs (204 methamphetamine-exposed and 208 unexposed matched comparisons) in the Infant Development, Environment, and Lifestyle study. The 151 children exposed to methamphetamine and 147 comparisons who attended the 7.5-year visit were included. Exposure was determined by maternal self-report and/or positive meconium toxicology. Maternal interviews assessed behavioral and cognitive outcomes using the Conners' Parent Rating Scale-Revised: Short Form.

**RESULTS:** After adjusting for covariates, children exposed to methamphetamine had significantly higher cognitive problems subscale scores than comparisons and were 2.8 times more likely to have cognitive problems scores that were above average on the Conners' Parent Rating Scale-Revised: Short Form. No association between prenatal methamphetamine exposure and behavioral problems, measured by the oppositional, hyperactivity, and attention-deficit/hyperactivity disorder index subscales, were found.

**CONCLUSIONS:** Prenatal methamphetamine exposure was associated with increased cognitive problems, which may affect academic achievement and lead to increased negative behavioral outcomes.

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J Psychopharmacol. 2014 Mar;28:179-203.

**EVIDENCE-BASED GUIDELINES FOR THE PHARMACOLOGICAL MANAGEMENT OF ATTENTION DEFICIT HYPERACTIVITY DISORDER: UPDATE ON RECOMMENDATIONS FROM THE BRITISH ASSOCIATION FOR PSYCHOPHARMACOLOGY.**

**Bolea-Alamanac B, Nutt DJ, Adamou M, et al.**

Attention deficit hyperactivity disorder (ADHD) is a common condition with a high societal burden. The present guidelines summarise current literature, generating expert consensus recommendations for the treatment of ADHD in children and adults. These guidelines also provide a review of recent research in the fields of neuroimaging, neuropsychology and genetics of ADHD. Novel discoveries in these areas have informed

physiological models for the disease. Since the publication of the previous British Association for Psychopharmacology guidelines in 2008, new drugs have been licensed and further compounds are being investigated. The publication of randomised controlled trials of psychological interventions has contributed to the range of treatment options for ADHD. As the disorder has been diagnosed more frequently there has been greater focus on comorbid conditions and how they impact treatment. Services have continued to develop for the treatment of ADHD in adults and care agreements have been introduced to facilitate access to treatment.

J Psychosoc Nurs Ment Health Serv. 2014 Feb;52:17-20.

**DISRUPTIVE MOOD DYSREGULATION DISORDER: A NEW DIAGNOSIS IN THE DSM-5.**

**Johnson K, McGuinness TM.**

This article explores a new diagnosis in the Diagnostic and Statistical Manual of Mental Disorders (5th ed.)-disruptive mood dysregulation disorder (DMDD). Frequent comorbidities of DMDD include oppositional defiant disorder and attention-deficit/hyperactivity disorder. The evolution of DMDD and how this diagnostic category may remedy an overdiagnosis of pediatric bipolar disorder are discussed.

JAMA Pediatr. 2014;168:1074-76.

**GEOGRAPHIC VARIATION IN RECEIPT OF PSYCHOTHERAPY IN CHILDREN RECEIVING ATTENTION-DEFICIT/HYPERACTIVITY DISORDER MEDICATIONS.**

**Gellad WF, Stein BD, Ruder T, et al.**

JAMA Psychiatry. 2014 Jul;71:786-96.

**EFFECT OF PRENATAL EXPOSURE TO TOBACCO SMOKE ON INHIBITORY CONTROL: NEUROIMAGING RESULTS FROM A 25-YEAR PROSPECTIVE STUDY.**

**Holz NE, Boecker R, Baumeister S, et al.**

**IMPORTANCE:** There is accumulating evidence relating maternal smoking during pregnancy to attention-deficit/hyperactivity disorder (ADHD) without elucidating specific mechanisms. Research investigating the neurobiological underpinnings of this disorder has implicated deficits during response inhibition. Attempts to uncover the effect of prenatal exposure to nicotine on inhibitory control may thus be of high clinical importance.

**OBJECTIVE:** To clarify the influence of maternal smoking during pregnancy (hereafter referred to as prenatal smoking) on the neural circuitry of response inhibition and its association with related behavioral phenotypes such as ADHD and novelty seeking in the mother's offspring.

**DESIGN, SETTING, AND PARTICIPANTS:** Functional magnetic resonance imaging was performed for the offspring at 25 years of age during a modified Eriksen flanker/NoGo task, and voxel-based morphometry was performed to study brain volume differences of the offspring. Prenatal smoking (1-5 cigarettes per day [14 mothers] or >5 cigarettes per day [24 mothers]) and lifetime ADHD symptoms were determined using standardized parent interviews at the offspring's age of 3 months and over a period of 13 years (from 2 to 15 years of age), respectively. Novelty seeking was assessed at 19 years of age. Analyses were adjusted for sex, parental postnatal smoking, psychosocial and obstetric adversity, maternal prenatal stress, and lifetime substance abuse. A total of 178 young adults (73 males) without current psychopathology from a community sample followed since birth (Mannheim, Germany) participated in the study.

**MAIN OUTCOMES AND MEASURES:** Functional magnetic resonance imaging response, morphometric data, lifetime ADHD symptoms, and novelty seeking.

**RESULTS:** Participants prenatally exposed to nicotine exhibited a weaker response in the anterior cingulate cortex ( $t_{168} = 4.46$ ; peak Montreal Neurological Institute [MNI] coordinates  $x = -2$ ,  $y = 20$ ,  $z = 30$ ; familywise error [FWE]-corrected  $P = .003$ ), the right inferior frontal gyrus ( $t_{168} = 3.65$ ; peak MNI coordinates  $x = 44$ ,  $y = 38$ ,  $z = 12$ ; FWE-corrected  $P = .04$ ), the left inferior frontal gyrus ( $t_{168} = 4.09$ ; peak MNI coordinates  $x = -38$ ,  $y = 36$ ,  $z = 8$ ; FWE-corrected  $P = .009$ ), and the supramarginal gyrus ( $t_{168} = 5.03$ ; peak MNI coordinates  $x = 64$ ,  $y = -$

28,  $z = 22$ ; FWE-corrected  $P = .02$ ) during the processing of the NoGo compared to neutral stimuli, while presenting a decreased volume in the right inferior frontal gyrus. These findings were obtained irrespective of the adjustment of confounders, ADHD symptoms, and novelty seeking. There was an inverse relationship between inferior frontal gyrus activity and ADHD symptoms and between anterior cingulate cortex activity and novelty seeking.

**CONCLUSIONS AND RELEVANCE:** These findings point to a functional involvement of prenatal exposure to tobacco smoke in neural alterations similar to ADHD, which underlines the importance of smoking prevention treatments.

J Abnorm Child Psychol. 2014 Nov;42:1353-65.

**SYMPTOMS OF ATTENTION-DEFICIT/HYPERACTIVITY DISORDER AND PEER FUNCTIONING: A TRANSACTIONAL MODEL OF DEVELOPMENT.**

**Tseng WL, Kawabata Y, Gau SS-F, et al.**

The goals of this short-term longitudinal study were to investigate differential, independent effects of inattention and hyperactivity/impulsivity on children's peer relationships and the dynamic, transactional interplay between ADHD symptoms and indices of peer functioning over time. This study used a community sample that included 739 preadolescents (239 fourth graders and 500 fifth graders; 52.23 % boys) from northern Taiwan, who were assessed every six months at three time points. Children's ADHD symptoms were measured using the parent report on the Swanson, Nolan, and Pelham, version IV scale. Positive and negative facets of peer functioning, including peer rejection, peer acceptance, and the number of friendships, were assessed via peer nomination. Results of cross-lagged models indicated that inattention, but not hyperactivity/impulsivity, predicted subsequent peer impairment (i.e., lower peer acceptance and fewer dyadic friendships). Findings also showed a vicious cycle in which inattentive symptoms predicted later peer impairment, which in turn led to increases in both inattention and hyperactivity/impulsivity. These findings did not differ across gender, and the majority of the findings remained significant even after controlling for age and physical aggression. Taken together, this study demonstrated the detrimental effect of inattention on children's peer functioning and the transactional and dynamic interplay between inattention and peer impairment in a Chinese culture.

J Abnorm Child Psychol. 2014 Nov;42:1407-12.

**EVALUATING CLINICALLY SIGNIFICANT CHANGE IN MOTHER AND CHILD FUNCTIONING: COMPARISON OF TRADITIONAL AND ENHANCED BEHAVIORAL PARENT TRAINING.**

**Rajwan E, Chacko A, Wymbs BT, et al.**

The Strategies to Enhance Positive Parenting (STEPP) program, an enhanced behavioral parent training (BPT) intervention, was developed to improve engagement in and outcomes following treatment for single-mother families of school-age youth with attention-deficit/hyperactivity disorder (ADHD). A previous randomized clinical trial of the STEPP program demonstrated that the intervention resulted in statistically significant improvements at the group-level in child oppositional behavior, various areas of child impairment, parental stress, and parenting behavior, relative to a wait-list control condition and a traditional BPT group. Despite benefits at the group-level, little is known about outcomes at the individual-level of enhanced BPT relative to traditional BPT for various child- and parent-level outcomes. The current study compares the extent to which traditional BPT and the STEPP program result in reliable change and recovery across various child- and parent-level outcomes in a sample of 80, 5–12 year old youth with ADHD (70 % male). Analyses demonstrated the benefit of participating in either BPT treatment; and participation in the STEPP program compared to traditional BPT was associated with only minimal incremental clinical benefit. Results, as well as clinical and research implications for assessment and treatment of high-risk families of youth with ADHD enrolled in BPT are discussed.

J Anxiety Disord. 2014;28:754-60.

**INATTENTION SYMPTOMS AND THE DIAGNOSIS OF COMORBID ATTENTION-DEFICIT/HYPERACTIVITY DISORDER AMONG YOUTH WITH GENERALIZED ANXIETY DISORDER.**

**Elkins RM, Carpenter AL, Pincus DB, et al.**

Generalized anxiety disorder (GAD) and attention-deficit/hyperactivity disorder (ADHD) commonly co-occur in childhood. Inattention symptoms can be hallmarks of both conditions, however assessment tools of inattention may not effectively distinguish between the two conditions. The present study used receiver operating characteristic (ROC) analyses to examine the high-end specificity of the Attention Problems Scale of the Child Behavior Checklist (CBCL) for detecting comorbid ADHD among youth with GAD (. N=. 46). Results support the utility of the Attention Problems Scale for accurately distinguishing between the two groups (AUC. = 84, SE. =.06). Specifically, a cut score of 63 achieved the most favorable values across diagnostic utility indices; 74% of GAD youth with ADHD scored above this cutoff and 91% of GAD youth without ADHD scored below this cutoff. Findings provide support for the use of the CBCL Attention Problems Scale to supplement diagnostic interviews and identify inattention associated with ADHD among GAD youth.

Journal of Attention Disorders. 2014 Nov;18:646-53.

**THE RELATIONSHIPS BETWEEN SENSORY MODULATION AND SLEEP AMONG ADOLESCENTS WITH ADHD.**

**Lufi D, Tzischinsky O.**

**Objective:** The purpose of this study was to investigate the effect of sensory modulation and sleeping among 30 adolescents diagnosed with ADHD, compared with 28 adolescents without ADHD.

**Method:** Two questionnaires were completed by parents to assess the participants' level of ADHD symptoms. Two other questionnaires were completed by the participants assessing difficulties in sensory modulation and sleep.

**Results:** The ADHD group had more sensory difficulties in Activity Level, Hearing, and Low Registration, and more difficulties in the Sleep Behavior variables. Higher correlations between the sensory variables and the sleep measures were found in the ADHD group as compared with the non-ADHD group. Significant differences between correlations were found between three sleep measures and four sensory variables.

**Conclusion:** The discussion is devoted to an assessment of the relationships between the measures, with the conclusion that among adolescents with ADHD, it is important to assess and treat possible sensory and sleep difficulties.

Journal of Attention Disorders. 2014 Nov;18:635-45.

**DO SYMPTOMS OF ADHD AT AGES 7 AND 10 PREDICT ACADEMIC OUTCOME AT AGE 16 IN THE GENERAL POPULATION?**

**Holmberg K, Bölte S.**

**Objective:** To examine the value of the Conners 10-item scale to predict academic outcomes at age 16 years in schoolchildren aged 7 and 10 years.

**Method:** A cohort study of N = 544 children in a municipality of Stockholm County was conducted. Using the parent and teacher version of the Conners 10-item scale, 7- and 10-year-olds were screened for ADHD symptoms and followed-up for school outcome at age 16 years.

**Results:** The best predictors for school outcome at age 16 years were the Conners items, "child failing to finish tasks" and "being inattentive, easily distracted," with a high specificity (90%-97%) but low sensitivity (18%-39%).

**Conclusion:** This study indicates a considerable association between certain symptoms of inattentiveness in young schoolchildren and academic underachievement at age 16 years. Screening for one to two symptoms of inattention in schoolchildren identifies 30% to 40% of participants at risk for later poor school attainment.



Journal of Attention Disorders. 2014 Nov;18:680-90.

**SUICIDAL BEHAVIORS IN ADOLESCENTS WITH ADHD: ASSOCIATIONS WITH DEPRESSIVE AND OTHER COMORBIDITY, PARENT–CHILD CONFLICT, TRAUMA EXPOSURE, AND IMPAIRMENT.**

**Daviss WB, Diler RS.**

**Objective:** To examine potential predictors of lifetime suicidal behaviors (SBs) in adolescents with ADHD.

**Method:** Participants were 101 adolescents with ADHD aged 11 to 18 years, evaluated for lifetime SB and psychopathology with semistructured interviews, and for lifetime trauma exposure, parent–child conflict, ADHD symptoms, and functional impairment with child, parent, and teacher ratings.

**Results:** Controlling for the effects of age, female sex, and comorbid depressive and other disorders, lifetime SB ( $n = 28$ ) remained significantly associated ( $p = .001$ ) with parent–child conflict, and to a lesser extent ( $p < .05$ ) with impairment in nonacademic domains of function and breadth of exposure to victimization events. Measures related to past and current ADHD symptoms and signs were not associated with lifetime SB.

**Conclusion:** Apart from depression, clinicians should pay particular attention to parent–child conflict, victimization trauma, and social impairment rather than levels of ADHD symptoms when weighing the likelihood of SB in youth with ADHD.

Journal of Attention Disorders. 2014 Nov;18:699-712.

**A PILOT STUDY OF THE EFFICACY OF A COMPUTERIZED EXECUTIVE FUNCTIONING REMEDIATION TRAINING WITH GAME ELEMENTS FOR CHILDREN WITH ADHD IN AN OUTPATIENT SETTING: OUTCOME ON PARENT- AND TEACHER-RATED EXECUTIVE FUNCTIONING AND ADHD BEHAVIOR.**

**Van der Oord S, Ponsioen AJG, Geurts HM, et al.**

**Objective:** This pilot study tested the short- and long-term efficacy (9 weeks follow-up) of an executive functioning (EF) remediation training with game elements for children with ADHD in an outpatient clinical setting, using a randomized controlled wait-list design. Furthermore, in a subsample, that is, those treated with methylphenidate, additive effects of the EF training were assessed.

**Method:** A total of 40 children (aged 8-12 years) were randomized to the EF training or wait-list. The training consisted of a 25-session training of inhibition, cognitive flexibility, and working memory. Treatment outcome was assessed by parent- and teacher-rated EF, ADHD, oppositional deviant disorder, and conduct disorder symptoms.

**Results:** Children in the EF training showed significantly more improvement than those in the wait-list condition on parent-rated EF and ADHD behavior in the total sample and in the subsample treated with methylphenidate. Effects were maintained at follow-up.

**Conclusion:** This pilot study shows promising evidence for the efficacy of an EF training with game elements.

J Autism Dev Disord. 2013;44:2707-16.

**CHILDHOOD NEURODEVELOPMENTAL DISORDERS AND VIOLENT CRIMINALITY: A SIBLING CONTROL STUDY.**

**Lundstrom S, Forsman M, Larsson H, et al.**

The longitudinal relationship between attention deficit hyperactivity disorder (ADHD) and violent criminality has been extensively documented, while long-term effects of autism spectrum disorders (ASDs), tic disorders (TDs), and obsessive compulsive disorder (OCD) on criminality have been scarcely studied. Using population-based registers of all child and adolescent mental health services in Stockholm, we identified 3,391 children, born 1984–1994, with neurodevelopmental disorders, and compared their risk for subsequent violent criminality with matched controls. Individuals with ADHD or TDs were at elevated risk of committing violent crimes, no such association could be seen for ASDs or OCD. ADHD and TDs are risk factors for subsequent violent criminality, while ASDs and OCD are not associated with violent criminality.

Journal of Child Psychology and Psychiatry. 2014 Nov;55:1244-50.

**CHILDREN'S RELATIVE AGE IN CLASS AND USE OF MEDICATION FOR ADHD: A DANISH NATIONWIDE STUDY.**

**Pottegård A, Hallas J, Hernández D, et al.**

**Background** Previous studies from North America and Iceland have shown that the youngest children within a grade are up to twice as likely to be diagnosed and treated for attention-deficit/hyperactivity disorder (ADHD) compared with their older classmates. We aimed to investigate whether younger age in class is associated with an increased probability of being prescribed medication for ADHD among school-aged children in Denmark.

**Methods** We followed all Danish children between 2000 and 2012 from 1st through 6th grade (7–12 years). Among children who started school on their age-assigned grade level, we estimated the prevalence proportion ratio (PPR) of receiving ADHD medication between the youngest children in class (born in October–December) and the oldest in class (born in January–March), specified by grade level, calendar year and gender. As a sensitivity analysis, we added children not on their age-assigned grade level to the main calculations.

**Results** We identified 932,032 eligible children for the main analysis, of whom 17.3% were among the youngest and 26.5% among the oldest in class. In total, 1.2% eligible children filled at least one prescription for ADHD medication in 2000–2012. The average PPR over the study period was 1.08 (95% CI, 1.04–1.12) and remained stable across subgroups and sensitivity analyses. Overall, 40% of children born October–December had entered school a year after their age-assigned grade level.

**Conclusions** Contrary to previous study results, we observed almost no relative age effect on medication use for ADHD among children in Denmark. We postulate that this may be due to the high proportion of relatively young children held back by 1 year in the Danish school system and/or a generally low prevalence of ADHD medication use in the country.

Journal of Clinical Nursing. 2014 Nov;23:3166-76.

**LIVING IN A FAMILY WITH A CHILD WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER: A PHENOMENOGRAPHIC STUDY.**

**Moen ØL, Hall-Lord ML, Hedelin B.**

**Aims and objectives:** To describe experiences of everyday life in families with a child with attention deficit hyperactivity disorder.

**Background:** Attention deficit hyperactivity disorder is a highly prevalent, clinically heterogeneous disorder characterised by behavioural symptoms of inattention, hyperactivity and impulsivity that creates impairments for the child and affects the family life. The impairments vary with age and context, and the same symptoms do not necessarily have the same effects in different contexts and persons.

**Design:** A qualitative design with a phenomenographic approach.

**Methods:** Family members, mothers, fathers, siblings and children with attention deficit hyperactivity disorder (n = 17) were interviewed individually.

**Results:** The findings include two descriptive categories 'safeguarding a functioning family' and 'fighting for acceptance and inclusion'. To create a stable and structured family life to avoid conflicts within the family and manage their daily life were crucial. The child with attention deficit hyperactivity disorder and their parents developed special skills and strategies to live with attention deficit hyperactivity disorder in the family sphere and the social context. To apply for help before the problems in the family become too severe and to share responsibility with professionals, who have competence, to meet the families in their worries were stressed. The striving in the family strengthened the companionship in the families, and they conceived growth.

**Conclusions:** This study contributes to knowledge of the parents, siblings and children with attention deficit hyperactivity disorder experiences of everyday life with a child with attention deficit hyperactivity disorder. All family members need support before their problems become too severe.

**Relevance to clinical practice:** There is a need of family-focused approach with a dialogue with family members to share the view of their situation and identify their individual resources and needs. Nurses should help these families with family supervision.

Journal of Experimental Child Psychology. 2014 Nov;127:126-43.

**EVENT- AND TIME-TRIGGERED REMEMBERING: THE IMPACT OF ATTENTION DEFICIT HYPERACTIVITY DISORDER ON PROSPECTIVE MEMORY PERFORMANCE IN CHILDREN.**

**Talbot KD, Kerns KA.**

The current study examined prospective memory (PM, both time-based and event-based) and time estimation (TR, a time reproduction task) in children with and without attention deficit hyperactivity disorder (ADHD). This study also investigated the influence of task performance and TR on time-based PM in children with ADHD relative to controls. A sample of 69 children, aged 8 to 13 years, completed the CyberCruiser-II time-based PM task, a TR task, and the Super Little Fisherman event-based PM task. PM performance was compared with children's TR abilities, parental reports of daily prospective memory disturbances (Prospective and Retrospective Memory Questionnaire for Children, PRMQC), and ADHD symptomatology (Conner's rating scales). Children with ADHD scored more poorly on event-based PM, time-based PM, and TR; interestingly, TR did not appear related to performance on time-based PM. In addition, it was found that PRMQC scores and ADHD symptom severity were related to performance on the time-based PM task but not to performance on the event-based PM task. These results provide some limited support for theories that propose a distinction between event-based PM and time-based PM.

J Forensic Psychiatry Psychol. 2014.

**CONTRASTING PSYCHOSOCIAL OUTCOMES IN CHINESE DELINQUENT ADOLESCENTS WITH ATTENTION DEFICIT AND HYPERACTIVITY DISORDER SYMPTOMS AND/OR READING DISABILITY.**

**Poon K, Suk-Han HC.**

Many studies reported high prevalence of attention deficit hyperactivity disorder (ADHD) and reading disability (RD) among delinquent adolescents. Very few have examined their psychosocial outcomes. The present study compared the psychosocial outcomes and delinquency outcomes in Chinese juvenile delinquents with ADHD symptoms (AS) and/or RD. Delinquents with AS (n = 29), RD (n = 24) and their comorbidity (n = 35) were recruited from juvenile institutions along with typically developing controls (n = 29) from local schools; all completed questionnaire on psychosocial characteristics and delinquency outcomes. Participants with AS were associated with poor academic orientation whereas participants with RD were characterized with negative main effects across all psychosocial constructs being tested. The comorbid group performed similar to the RD group yet it exhibited a significantly higher delinquency severity. The present findings provide a better picture of the unique psychosocial profile associated with different groups, allowing for better matching for future identification and intervention programme.

Journal of Marital and Family Therapy. 2014 Oct;40:509-24.

**YOUNG ADULT ROMANTIC COUPLES' CONFLICT RESOLUTION AND SATISFACTION VARIES WITH PARTNER'S ATTENTION-DEFICIT/HYPERACTIVITY DISORDER TYPE.**

**Canu WH, Tabor LS, Michael KD, et al.**

Attention-deficit/hyperactivity disorder (ADHD) has previously been associated with less satisfaction and success in romantic relationships. This study compares conflict resolution and problem-solving behaviors in young adult romantic couples either having one partner with ADHD combined type (C-couples), having one partner identified with ADHD inattentive type (IA-couples), or in which neither partner has an ADHD diagnosis (nondiagnosed [ND] couples). Self-reports of current and childhood ADHD symptoms corroborated diagnostic status and speaker and listener behaviors, coded via the Rapid Couples Interaction Scoring System (Gottman, 1996), were the primary dependent variables. Analyses revealed greater negativity and less positivity in C-couples' behavior during a conflict resolution task, relative to IA and ND couples, and this corresponded with couples' relational satisfaction. IA-couples emitted relational behavior that was largely similar to ND couples. Findings support that relational impairment exists in C-couples, and to some degree, contrast with previous research suggesting that individuals

with predominant inattention experience greater social impairment in adulthood than those with other types of ADHD.

J Popul Ther Clin Pharmacol. 2014;21:e357-e369.

**IMPACT OF A RESTRICTIVE DRUG ACCESS PROGRAM ON THE RISK OF CARDIOVASCULAR ENCOUNTERS IN CHILDREN EXPOSED TO ADHD MEDICATIONS.**

**Guertin J, LeLorier J, Durand M, et al.**

**Background:** ADHD medications increase clinical encounters for cardiovascular symptoms. Uncertain are the roles of differences in ADHD medications and restrictive practices by drug programs

**Methods:** We conducted two nested case-control studies. The first was nested within a cohort of children de novo users of methylphenidate, amphetamines or atomoxetine and the second case-control study was nested within a subcohort of de novo amphetamine or atomoxetine users with no cardiovascular events prior to the first dispensing of either drug. The outcome for both studies was the composite of physician visits, emergency room visits or hospitalizations for cardiovascular reasons. Cases were matched on sex, age and date of entry within the cohorts, with up to 10 controls. Patients with an active dispensation of ADHD medications at the index date (and up to 90 days previously) were considered exposed. Conditional logistic regression was used to calculate odd ratios (OR)

**Results:** The full cohort comprised 38,495 patients. Among these patients, 3595 (9.3%) had no prior cardiovascular events (the subcohort). In the full cohort, an association was demonstrated with exposure to amphetamine and atomoxetine (but not methylphenidate) and the cardiovascular encounter outcomes. When the sub-cohort was analyzed the associations with amphetamine or atomoxetine were no longer evident

**Conclusion:** Reimbursement policies need to be considered when conducting observational studies. Had the analysis been conducted without consideration of these policies the results would have incorrectly identified amphetamine and atomoxetine as important risk factors for cardiovascular encounters.

Journal of Psychiatric and Mental Health Nursing. 2014 Sep;21:601-08.

**DETERMINING THE CORRELATION BETWEEN QUALITY OF LIFE AND SELF-CONCEPT IN CHILDREN WITH ATTENTION DEFICIT/HYPERACTIVITY DISORDER.**

**Dolgun G, Savaser S, Yazgan Y.**

This study was conducted to determine the relationship between how children with attention deficit/hyperactivity disorder (ADHD) perceive their quality of life and their self-concept. The study involved descriptive/correlational research with 70 children, ages 9–12 with ADHD. Data were collected with the ADHD Quality of Life Scale (ADHD/QoLS) and the Piers–Harris Children's Self-Concept Scale (PHCSCS). Data were assessed using Pearson's and Spearman's correlation analysis; the level of significance was accepted as  $P < 0.05$ . The analysis of the data determined that there was a significant relationship between all of the domains of the Self-Concept Scale and ADHD/QoLS and its subscales ( $P < 0.001$ ). An evaluation of the correlation analysis for the relationship between ADHD/QoLS and PHCSCS and their subscales revealed that there was a strong, positive and very significant relationship between ADHD and self-concept, both at school and at home.

J Psychosom Res. 2014;77:316-21.

**IS ATOPY IN EARLY CHILDHOOD A RISK FACTOR FOR ADHD AND ASD? A LONGITUDINAL STUDY.**

**Chen M-H, Su T-P, Chen Y-S, et al.**

**Objective:** Previous studies have found a temporal concordance in the increased prevalence of atopic diathesis/atopic diseases, attention-deficit hyperactivity disorder (ADHD), and autistic spectrum disorder (ASD) worldwide. But, the temporal association among these 3 distinct diseases is unknown.

**Method:** 14,812 atopic subjects diagnosed with any atopic disease (asthma, atopic dermatitis, allergic rhinitis, or allergic conjunctivitis) before the age of 3 (atopic cohort) and 6944 non-atopic subjects with no lifetime atopic

disease (non-atopic cohort), born between 1997 and 2000, were enrolled and followed to December 31, 2010 to identify the development of ADHD and ASD.

**Results:** The presence of any atopic disease in early childhood increased the risk of developing ADHD (hazard ratio [HR]: 1.97) and ASD (HR: 3.40) in later life. Greater numbers of atopic comorbidities (4 comorbidities: ADHD: HR: 2.53; ASD: HR: 4.29) were significantly related to a greater risk of developing ADHD and ASD.

**Discussion:** Atopic diathesis in early childhood elevated the risk of developing ADHD and ASD in later life, with the dose-dependent relationship of more atopic comorbidities with a greater likelihood of ADHD and ASD.

J Am Acad Audiol. 2014;25:676-87.

**ATTEND TO THIS: THE RELATIONSHIP BETWEEN AUDITORY PROCESSING DISORDERS AND ATTENTION DEFICITS.**

**Gyldenkaerne P, Dillon H, Sharma M, et al.**

**Background:** Children clinically diagnosed with auditory processing disorders (APDs) are often described as easily distracted and inattentive, leading some researchers to propose that APDs might be a consequence of underlying attention difficulties or a subtype of attention disorders.

**Purpose:** The aim of this study was to investigate the link between AP and attention by determining the relationship between performance on an auditory and visual sustained attention task and performance on a common APD test battery.

**Research Design:** This study was a cross-sectional correlation study of school-aged children.

**Study Sample:** Participants were a clinical group of 101 children considered by their parents or teachers to have listening difficulties, and a control group of 18 children with no suspected listening difficulties. All children were 7-12 yr old.

**Data Collection and Analysis:** All children passed a standard peripheral audiologic assessment and were assessed using a clinical APD test battery and reading accuracy, nonverbal intelligence, and visual and auditory continuous performance tests.

**Results:** There were significant correlations within the APD test scores except for masking level difference values, which did not correlate significantly with any other measure. Dichotic Digit and Frequency Pattern scores also correlated significantly with Nonverbal Intelligence and Sustained Auditory and Visual Attention scores. Within the clinical group, there were twice as many children outside normal limits on both the APD test battery and the attention tests as there were children who were outside normal limits on only the APD test battery or only the attention tests. Significant predictors of reading ability were the Frequency Pattern, Gaps In Noise, and Nonverbal Intelligence scores.

**Conclusions:** The degree of correlation between the APD and attention measures indicates that although deficits in both AP and sustained attention co-occur in some children (more than would be expected from chance alone), and the two conditions may have similar symptoms, they are separate, largely independent conditions.

Kathmandu Univ Med J (KUMJ ). 2013 Jul;11:191-95.

**STUDY ON DEVELOPMENTAL-BEHAVIOURAL PEDIATRICS TRAINING EXPERIENCES OF PEDIATRICIANS AND PEDIATRIC TRAINEES WORKING IN NEPAL.**

**Rimal HS, Pokharel A, Saha V.**

**BACKGROUND:** There are growing concerns about developmental, behavioural, social and emotional wellbeing of children throughout the world. A huge gap exists between the instructions provided on medical disciplines and on areas of Developmental-Behavioural Pediatrics (DBP) during pediatric training in our region.

**OBJECTIVE:** This study aims to evaluate the Developmental-Behavioural pediatrics (DBP) training experiences of pediatricians and pediatric trainees during their post graduate training in pediatrics.

**METHODS:** Questionnaires were sent to the pediatricians / trainees and data was analyzed using SPSS software.

**RESULT:** More than 56 % of respondents were satisfied in 10 out of 11 medical disciplines whereas more than 56% were unsatisfied in 10 out of 11 developmental behavioural pediatrics disciplines. This study has demonstrated that between 50-60 % of pediatricians did not see the cases of ADHD, learning difficulty and



family dysfunction for a period of three months prior to the survey which are relatively common conditions. Even in post graduate training nearly 66 % of pediatricians were unsatisfied with their instructions in DB pediatrics.

**CONCLUSION:** Pediatricians working in Nepal have difficulties in addressing the issues of developmental pediatrics, raising a question about the need to review the curriculum of post graduate training in Pediatrics.

Konuralp Derg. 2014;6:21-26.

**INVESTIGATION OF PREVALENCE OF ATTENTION DEFICIT HYPERACTIVITY DISORDER AMONG ADOLESCENTS.**

**Uyan Z, Peker AGC, Tekiner AS, et al.**

**Aim:** Attention deficit hyperactivity disorder (ADHD) is the most common neurobehavioral disorder of childhood and adolescence. The aim of this study is to investigate the prevalence of ADHD with oppositional defiant disorder (ODD) and conduct disorder (CD) which may accompany to ADHD according to parent and teacher statements.

**Method:** This cross-sectional research involving 251 adolescents from 9 different schools in Ankara was carried out between April and June 2007. Adolescents were assessed in Child and Adolescent Behavior Disorders Screening and Rating Scale based on DSM-IV. A questionnaire was used for sociodemographic attributes. Screening and rating scale was completed by both class teacher and parent of the students.

**Results:** According to the combined statements of parent and teacher 5.9% of the students had ADHD symptoms. The prevalence of ADHD was 12.7% and 27.4% on the basis of parent and teacher reports respectively. ADHD symptoms were significantly higher among boys on the basis of both teacher and parent reports ( $p < 0.001$ ). There was no significant difference between ADHD symptoms and socioeconomic status and parent education level. The prevalence of ODD was 46.4% and 52.5% among adolescents with ADHD symptoms according to parent and teacher assessments respectively.

**Conclusion:** Informing parent and teachers about DEHB and other disruptive behaviors, and about the outcomes due these problems is important in view of early recognition of the problem, initiation of treatment and being supportive for the adolescent.

Lakartidningen. 2014 Aug;111:1350, 1352.

**PARACETAMOL FOR CHILDREN AND PREGNANT--THE PRECAUTIONARY PRINCIPLE SHOULD PREVAIL. BE CAUTIOUS WITH PARACETAMOL WHILE THE RISK FOR ADHD AND ASTHMA IS BEING INVESTIGATED.**

**Axelsson I.**

Med Sci Monit. 2014;20:608-13.

**DISRUPTIVE PATTERNS OF EATING BEHAVIORS AND ASSOCIATED LIFESTYLES IN MALES WITH ADHD.**

**Ptacek R, Kuzelova H, Stefano GB, et al.**

**BACKGROUND:** Attention deficit hyperactivity disorder (ADHD) is a neurological/behavioral disorder characterized by inattention or hyperactivity and impulsivity, or combined symptomatology. Children with ADHD are predisposed to irregular and/or impulsive eating patterns often leading to compromised physical condition. The goal of the present study was to statistically evaluate parental scoring of patterned eating behaviors and associated lifestyles within a cohort of 100 boys diagnosed with ADHD in comparison to age-matched male controls.

**MATERIAL AND METHODS:** The study population consisted of 100 boys aged 6-10 years diagnosed with mixed type ADHD by DSM-IV criteria and 100 age-matched healthy male control subjects. Patterns of eating behaviors and associated lifestyles were scored by structured parental interviews using a nominal rating scale.

**RESULTS:** Interview scores indicated statistically significant differences in patterned eating behaviors in subjects with ADHD in comparison to healthy controls. Notably, subjects diagnosed with ADHD exhibited markedly diminished adherence to a traditional breakfast, lunch, and dinner schedule, which was linked to a significantly higher frequency ( $>5/\text{day}$ ) of irregular eating times. In the ADHD cohort, disruptive patterns of eating



behaviors were associated with diminished nutritional value of ingested food (expressed as lowered content of fruits and vegetables) and increased consumption of sweetened beverages. **CONCLUSIONS:** Disruptive patterns of eating behaviors, metabolically unfavorable nutritional status, and diminished physical activities of male children diagnosed with ADHD are linked to compromised growth and development and appearance of metabolic diseases in adulthood.

MMW Fortschr Med. 2014 Aug;156:41-44.

**ATTENTION DEFICIT HYPERACTIVITY DISORDER IN CHILDREN AND ADOLESCENTS.**

**Mehler-Wex C, Deimel W.**

Natl Bur Econ Res Bull Aging Health. 2014;1-2.

**THE EFFECTS OF STIMULANT MEDICATIONS FOR ADHD.**

*Anon.*

Neuropsychiatr. 2014;28:97-99.

**IS ADHD OVERDIAGNOSED? (INTERVIEW BY DR. ALEXANDER LINDEMEIER).**

**Hackenberg B, Kienbacher C.**

Neuropsychiatr Dis Treat. 2014;10:2039-47.

**POST HOC ANALYSES OF THE IMPACT OF PREVIOUS MEDICATION ON THE EFFICACY OF LISDEXAMFETAMINE DIMESYLATE IN THE TREATMENT OF ATTENTION-DEFICIT/ HYPERACTIVITY DISORDER IN A RANDOMIZED, CONTROLLED TRIAL.**

**Coghill DR, Banaschewski T, Lecendreux M, et al.**

**Background:** Following the approval of lisdexamfetamine dimesylate (LDX) in several European countries for the treatment of attention-deficit/hyperactivity disorder (ADHD) in children and adolescents with an inadequate response to methylphenidate (MPH) treatment, the aim of the present analysis was to establish the response to LDX in subgroups of patients with different ADHD medication histories

**Methods:** This was a post hoc subgroup analysis of data from a 7-week, European, double-blind, dose-optimized, Phase III study. Patients aged 6-17 years were randomized 1:1:1 to LDX, placebo, or osmotic-release oral system methylphenidate (OROS-MPH). OROS-MPH was included as a reference arm rather than as a direct comparator. Efficacy was assessed in patients categorized according to their ADHD medication history using the ADHD Rating Scale IV and Clinical Global Impressions-Improvement (CGI-I) scores

**Results:** The difference between active drug and placebo in least-squares mean change from baseline to endpoint in ADHD Rating Scale IV total score (95% confidence interval) was similar between the overall study population (n=317; LDX, -18.6 [-21.5, -15.7]; OROS-MPH, -13.0 [-15.9, -10.2]) and treatment-naïve individuals (n=147; LDX, -15.1 [-19.4, -10.9]; OROS-MPH, -12.7 [-16.8, -8.5]) or patients previously treated with any ADHD medication (n=170; LDX, -21.5 [-25.5, -17.6]; OROSnullMPH, -14.2 [-18.1, -10.3]). In addition, similar proportions of patients receiving active treatment were categorized as improved based on CGI-I score (CGI-I of 1 or 2) in the overall study population and among treatment-naïve individuals or patients previously treated with any ADHD medication

**Conclusion:** In these post hoc analyses, the response to LDX treatment, and to the reference treatment OROS-MPH, was similar to that observed for the overall study population in subgroups of patients categorized according to whether or not they had previously received ADHD medication.

Neuropsychologia. 2014;63:51-58.

**HEMODYNAMIC RESPONSE OF CHILDREN WITH ATTENTION-DEFICIT AND HYPERACTIVE DISORDER (ADHD) TO EMOTIONAL FACIAL EXPRESSIONS.**

**Ichikawa H, Nakato E, Kanazawa S, et al.**

Children with attention-deficit/hyperactivity disorder (ADHD) have difficulty recognizing facial expressions. They identify angry expressions less accurately than typically developing (TD) children, yet little is known about their atypical neural basis for the recognition of facial expressions. Here, we used near-infrared spectroscopy (NIRS) to examine the distinctive cerebral hemodynamics of ADHD and TD children while they viewed happy and angry expressions. We measured the hemodynamic responses of 13 ADHD boys and 13 TD boys to happy and angry expressions at their bilateral temporal areas, which are sensitive to face processing. The ADHD children showed an increased concentration of oxy-Hb for happy faces but not for angry faces, while TD children showed increased oxy-Hb for both faces. Moreover, the individual peak latency of hemodynamic response in the right temporal area showed significantly greater variance in the ADHD group than in the TD group. Such atypical brain activity observed in ADHD boys may relate to their preserved ability to recognize a happy expression and their difficulty recognizing an angry expression. We firstly demonstrated that NIRS can be used to detect atypical hemodynamic response to facial expressions in ADHD children.

No To Hattatsu. 2014;46:359-62.

**A CASE OF LARGE ARTERIOVENOUS MALFORMATION IN THE FRONTAL LOBE COMPLICATING ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.**

**Nakamura Y, Shimazaki M, Komatsu Y, et al.**

We report a 4-year old boy with a large arteriovenous malformation (AVM) exhibiting attention-deficit hyperactivity disorder (AD/HD). He presented with hyperkinesia at the age of 3 years and jacksonian seizure at 3 years 11 months, when he was diagnosed as AVM by cranial computed tomography. Magnetic resonance imaging revealed an AVM of 6 cm in diameter in the left frontal lobe. After 1 year, the AVM developed a varix, and both were surgically removed. We speculate that the prefrontal area was affected by direct compression from AVM and chronic ischemia due to steal phenomenon. Although AD/HD is rarely caused by parenchymal lesions, such as AVM, physicians should carefully investigate causative lesions.

Osaka City Med J. 2014 Jun;60:1-10.

**PSYCHIATRIC COMORBIDITY IN CHILDREN WITH HIGH-FUNCTIONING PERVASIVE DEVELOPMENTAL DISORDER.**

**Kusaka H, Miyawaki D, Nakai Y, et al.**

**BACKGROUND:** In previous studies for children with pervasive developmental disorder (PDD), the prevalence for psychiatric comorbidities has varied because of their methodological differences. In this research, our PDD subjects were strictly limited by age and IQ scores, and we utilized a semi-structured interview to diagnose their coexisting disorders. The purpose of this study is to identify reliable prevalence and types of psychiatric comorbidities in children with high-functioning PDD (HFPDD).

**METHODS:** The subjects were 49 children aged 6-15 years with HFPDD. In order to diagnose the comorbidities among them, we used the Japanese version of the Schedule for Affective Disorders and Schizophrenia for School-Age Children-Present and Lifetime version.

**RESULTS:** Forty-eight cases (98%) met the criteria for at least one comorbidity. The median number of the present comorbidities per child was 2, and the mode was 2. Depression (37%), attention deficit hyperactivity disorder (49%), and oppositional defiant disorder (45%) were frequently observed.

**CONCLUSIONS:** Our finding indicates the high prevalence of comorbidities and the variety of the comorbid disorders in children with HFPDD. It is important to be aware of those comorbid disorders to provide the children with effective treatments.

Pain. 2014 Apr;155:821-27.

**THE EFFECTS OF MENSTRUAL-RELATED PAIN ON ATTENTIONAL INTERFERENCE.**

**Keogh E, Cavill R, Moore DJ, et al.**

Pain-related attentional interference has been found in both chronic pain and laboratory-induced pain settings. However, few studies have examined such interference effects during common everyday painful episodes. Menstrual cycle-related pain is a common pain that affects a large number of women on a regular basis. The purpose of the current study was, therefore, to examine the effects of menstrual pain on attentional interference. Fifty-two healthy adult women were tested during 2 different phases of their menstrual cycles: once during a nonpain phase (mid follicular), and once while experiencing menstrual pain (late luteal/early follicular). On each testing session, participants received a battery of 4 attentional interference tasks that included selective attention (flanker task), attention span (n-back task), attentional switching (switching task), and divided attention (dual task). Greater attentional interference effects were found to occur during the menstrual pain phase compared to the nonpain phase. Interestingly, the nature of this effect was a general worsening in performance (e.g., slowing, less accurate), rather than a specific attentional deficit. These results add to a growing literature that generally indicates that attentional interference occurs across a range of different types of pain, including common painful episodes. However, they also highlight that the specific nature of this interference effect may depend on the type pain under consideration. Implications of these findings are also considered.

Pathol Biol. 2014;62:319-31.

**THE EFFECT OF SLEEP RESTRICTION ON NEUROBEHAVIOURAL FUNCTIONING IN NORMALLY DEVELOPING CHILDREN AND ADOLESCENTS: INSIGHTS FROM THE ATTENTION BEHAVIOUR AND SLEEP LABORATORY.**

**Cassoff J, Bhatti JA, Gruber R.**

In the current paper, we first introduce the research themes of the attention, behaviour and sleep (ABS) laboratory, namely, sleep and ADHD, sleep and obesity, and sleep and academic performance. We then focus in on the topic to be reviewed in the current paper-the association between sleep restriction and neurobehavioral functioning (NBF) in typically developing children. We review the research thus far conducted by the ABS lab specific to this topic and posit the unique methodological contributions of the ABS lab (e.g. home-based assessment of sleep architecture and patterns, extensive phenotyping, etc.) in terms of advancing this research area. In the second section of the paper, we review 13 studies investigating the causal association between experimental sleep restriction and NBF in normally developing pediatric populations. Eight of the 13 studies found that sleep restriction causes impairments in neurobehavioural functioning. However, given the inconsistency in outcome measures, experimental protocols and statistical power, the studies reviewed herein are difficult to interpret. Strategies used by the ABS including implementing home assessments of sleep, restricting sleep relative to the participants' typical sleep schedules, blinding raters who assess NBF, and using valid and reliable NBF assessments

are an attempt to address the gaps in this research area and clarify the causal relationship between sleep restriction and NBF in typically developing children and adolescents.

Pediatr Dermatol. 2014;31:614-15.

**GUANFACINE-INDUCED LICHENOID DRUG ERUPTION IN A CHILD WITH AUTISM AND ATTENTION DEFICIT HYPERACTIVITY DISORDER.**

**Romanelli M, Rhodes A .**

Lichenoid drug eruptions (LDEs) have a variety of medication causes. We report a case of a 5-year-old boy with autism and attention deficit hyperactivity disorder treated with guanfacine who developed pruritic lesions consistent with LDEs. Rechallenge was not attempted. There are several clinical and histopathologic clues that may distinguish LDEs from lichen planus

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Pediatrics. 2014 Jun;133:1070-80.

**STIMULANT TREATMENT OF ADHD AND CIGARETTE SMOKING: A META-ANALYSIS.**

**Schoenfelder EN, Faraone SV, Kollins SH.**

**BACKGROUND AND OBJECTIVE:** Individuals with attention-deficit/hyperactivity disorder (ADHD) have a significantly higher risk of cigarette smoking. The nature of the relationship between smoking and psychostimulant medications commonly used to treat ADHD is controversial. Our objective was to examine the relationship between stimulant treatment of ADHD and cigarette smoking by using meta-analysis, and to identify study and sample characteristics that moderate this relationship.

**METHODS:** Literature searches on PubMed and PsycInfo databases identified published studies for inclusion. Included studies compared cigarette smoking outcomes for stimulant-treated and untreated ADHD individuals. Seventeen studies met inclusion criteria, and 14 (total n = 2360) contained sufficient statistical information for inclusion in the meta-analysis. Two authors extracted odds ratios or frequencies of smokers in the treatment or nontreatment groups, and coded study characteristics including sample source, percentage of male participants, follow-up length, treatment consistency, type of smoking measure, prospective study, and controlling for comorbidities.

**RESULTS:** Meta-analysis revealed a significant association between stimulant treatment and lower smoking rates. Meta-regression indicated that effect sizes were larger for studies that used clinical samples, included more women, measured smoking in adolescence rather than adulthood, conceptualized stimulant treatment as consistent over time, and accounted for comorbid conduct disorder.

**CONCLUSIONS:** Nearly all studies were naturalistic, precluding causal inferences. Available data were insufficient to examine additional influences of patient demographics, treatment effectiveness, or other comorbidities. Consistent stimulant treatment of ADHD may reduce smoking risk; the effect was larger in samples with more severe psychopathology. Implications for further research, treatment of ADHD, and smoking prevention are discussed.

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Pediatrics. 2014 Sep;134:563-70.

**SMALL GEOGRAPHIC AREA VARIATIONS IN PRESCRIPTION DRUG USE.**

**Weinstein SJ, House SA, Chang CH, et al.**

**BACKGROUND:** Despite the frequency of pediatric prescribing little is known about practice differences across small geographic regions and payer type (Medicaid and commercial).

**OBJECTIVE:** The goal of this research was to quantify variation in prescription drug use among northern New England children.

**METHODS:** Northern New England, all-payer administrative data (2007-2010) permitted study of prescriptions for 949 821 children ages 0 to 17 years (1.75 million person-years [PYs]; 54% Medicaid, 46% commercial). Age- and gender adjusted overall and drug group-specific prescription use was quantified according to payer type (Medicaid or commercial) and within payer type across 69 hospital service areas (HSAs). We measured prescription fills per PY (rate) and annual, mean percentage of the population with any drug group-specific fills (prevalence).

**RESULTS:** Overall mean annual prescriptions per PY were 3.4 (commercial) and 5.5 (Medicaid). Generally, these payer type differences were smaller than HSA-level variation within payer type. HSA-level rates of

attention-deficit/hyperactivity disorder drug use (5th-95th percentile) varied twofold in Medicaid and more than twofold in commercially insured children; HSA-level antidepressant use varied more than twofold within each payer type. Antacid use varied threefold across HSAs and was highest in infants where commercial use paradoxically exceeded Medicaid. Prevalence of drug use varied as much as rates across HSAs.

**CONCLUSIONS:** Prescription use was higher among Medicaid-insured than commercially insured children. Regional variation generally exceeded payer type differences, especially for drugs used in situations of diagnostic and therapeutic uncertainty. Efforts should advance best pediatric prescribing discussions and shared decision-making.

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Physiol Behav. 2014.

**OBJECTIVE ASSESSMENT OF ADHD CORE SYMPTOMS IN CHILDREN WITH HEAVY PRENATAL ALCOHOL EXPOSURE.**

**Infante MA, Moore EM, Nguyen TT, et al.**

Attention deficits are often observed in children with prenatal alcohol exposure and attention-deficit/hyperactivity disorder (ADHD) is commonly diagnosed in this population. This study used an objective assessment tool to examine differences between alcohol-exposed and non-exposed children on core symptoms of ADHD: inattention, impulsivity, and hyperactivity. Two groups of individuals, aged 7-14. years, participated in the study: alcohol-exposed children (AE, n = 43), and non-exposed children (CON, n = 54). Subjects were evaluated with the Quotient ADHD System, which provides objective data on ADHD core symptoms by combining an infrared motion tracking system and a computerized continuous performance task. Twelve separate ANCOVAs controlling for the effects of age and sex, were conducted on attention and motion variables. Results revealed that in comparison to the CON group, the AE group was significantly (p's .05) less accurate, made an increased number of omission errors, had longer response latencies, and increased variability in response time. Moreover, the AE group spent less time staying still, and made an increased number of head movements, which traveled a larger distance, covered a greater area, and demonstrated a less complex movement pattern. No significant group differences were observed on the number of commission errors and temporal scaling. Our findings provide further support for the notion that inattention is a core deficit in children prenatally exposed to alcohol. Results from this study are also consistent with parent reports of increased hyperactivity. The Quotient ADHD System may be a useful objective measure of ADHD symptomatology in children with FASD.

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Presse Med. 2014 Sep;43:912-20.

**BIPOLAR DISORDER IN CHILDREN AND ADOLESCENTS: A DIFFICULT DIAGNOSIS.**

**Geoffroy PA, Jardri R, Etain B, et al.**

Bipolar disorder (BD) is a severe mental condition with neurodevelopmental features that clinically results in pathological fluctuations of mood. Whereas it was classically or traditionally considered as an adult-onset disorder, recent findings suggest that BD may occur very early in the life course, thus, determining what is now called Juvenile bipolar disorder (JBD). One of the reasons for which JBD has been so difficult to identify is that JBD primary symptoms vary much from the typical adulthood BD clinical expression. Euphoric mood is rare in JBD, while irritability mood, aggressive temper, mixed manic state onset, rapid cycling, anger outbursts and chronic course of symptoms are much more frequent. This specific clinical presentation makes JBD difficult to differentiate from other diagnoses related to pathological externalizing behaviours, including conduct disorder, oppositional provocative disorder, and attention deficit-hyperactivity disorder.

Prog Neuro-Psychopharmacol Biol Psychiatry. 2015;57:132-39.

**SYNAPTOSOME-RELATED (SNARE) GENES AND THEIR INTERACTIONS CONTRIBUTE TO THE SUSCEPTIBILITY AND WORKING MEMORY OF ATTENTION-DEFICIT/HYPERACTIVITY DISORDER IN MALES.**

**Gao Q, Liu L, Chen Y, et al.**

**Backgrounds:** N-ethylmaleimide-sensitive attachment protein receptor (SNARE) complex involved in neurotransmission via exocytosis was implicated in attention-deficit/hyperactivity disorder (ADHD). The present study investigated the influence of SNARE related genes and their interaction on ADHD susceptibility and their cognitive functions.

**Methods:** We genotyped eight single nucleotide polymorphisms (SNP) of Syntaxin 1A (STX1A), vesicle-associated membrane protein 2 (VAMP2) and synaptosomal-associated protein 25. kDa (SNAP25) and conducted case-control studies in 1404 male ADHD and 617 male controls. Quantitative analyses were performed for genotypes and performance on the Rey-Osterrieth complex figure test (RCFT), digit span test and Stroop test in 383 ADHD males. In addition, we explored gene-gene interactions by generalized multifactor dimensionality reduction (GMDR) followed with logistic regression and analyses of covariance for verifying.

**Results:** Genotypic distribution of rs875342 of STX1A was significantly different between ADHD and controls. The SNPs, rs363039 of SNAP25 and rs1150 of VAMP2, were significantly associated with RCFT scores, while rs875342 of STX1A with digit span. We found genetic interaction models between these three genes and ADHD susceptibility as well as working memory function evaluated by RCFT.

**Conclusion:** SNARE complex genes and their interactions may play a significant role in susceptibility and working memory of ADHD. (bullet)SNARE complex was critical in fusion and showed association with psychiatric disorders, including ADHD.

Psychiatry Res. 2014;220:426-32.

**EMOTIONAL REACTIVITY IN REFERRED YOUTH WITH DISRUPTIVE BEHAVIOR DISORDERS: THE ROLE OF THE CALLOUS-UNEMOTIONAL TRAITS.**

**Masi G, Milone A, Pisano S, et al.**

Deficits in emotional reactivity are frequently reported in Disruptive Behavior Disorders (DBDs). A deficit in prosocial emotions, namely the callous unemotional traits (CU), may be a mediator of emotional reactivity. Our aim is to investigate subjective emotional reactivity towards visual stimuli with different affective valence in youths with DBDs and healthy controls. The clinical sample included 62 youths with DBDs (51 males, 8 to 16 years, mean 11.3 (plus or minus) 2.1 years), the control group 53 subjects (36 males, 8 to 16 years, mean 10.8 (plus or minus) 1.5 years). The groups were compared using the Child Behavior Checklist (CBCL), the Inventory of Callous-Unemotional Traits (ICU), and the International Affective Picture System (IAPS), which explores the affective (pleasant/unpleasant emotional reaction) and arousal (low/high intensity of emotion) dimensions. The DBD group presented higher scores in externalizing and internalizing CBCL scores, and in ICU callous and indifferent subscales. At the IAPS, DBD patients differed from controls in the affective valence of the images, rating less unpleasant neutral and negative images. The CU traits were the only predictor of emotional reactivity in the DBD sample. A less aversive way to interpret neutral and negative stimuli may explain why DBD patients are less responsive to negative reinforcements

Psychiatry Res. 2014;220:708-10.

**ASSOCIATION BETWEEN GUC2C AND ADHD: EVIDENCE FROM BOTH CATEGORICAL AND QUANTITATIVE TRAITS.**

**Liu L, Li H, Wang Y, et al.**

Guanylyl cyclase-C knock-out mice exhibit hyperactivity and attention deficits. We investigated seven single nucleotide polymorphisms (SNPs) of Guanylate cyclase 2C gene (GUC2C) in 381 ADHD trios and 382 healthy controls. Transmission disequilibrium tests (TDT), case-control studies and quantitative analyses indicated association between GUC2C with ADHD and its core symptoms.



Psychiatry Res Neuroimaging. 2014;224:112-18.

**A MULTIMODAL MRI STUDY OF THE HIPPOCAMPUS IN MEDICATION-NAIVE CHILDREN WITH ADHD: WHAT CONNECTS ADHD AND DEPRESSION?**

**Posner J, Siciliano F, Wang Z, et al.**

Children with attention-deficit/hyperactivity disorder (ADHD) are at increased risk for developing depression. The neurobiological substrates that convey this risk remain poorly understood. On the basis of considerable data implicating hippocampal abnormalities in depressive disorders, we aimed to explore the relationship between the hippocampus and levels of depressive symptomatology in ADHD. We used magnetic resonance imaging (MRI) to examine the volumes and resting-state functional connectivity of the hippocampus in a sample of 32 medication naive children with ADHD (ages 6 - 13) and 33 age- and sex-matched healthy control (HC) participants. Compared with the HC participants, the participants with ADHD had (i) reduced volumes of the left hippocampus and (ii) reduced functional connectivity between the left hippocampus and the left orbitofrontal cortex (OFC); these hippocampal effects were associated with more severe depressive symptoms, even after controlling for the severity of inattentive and hyperactive/impulsive symptoms. Altered hippocampal structure and connectivity were not associated with anxiety or more general internalizing symptoms. Though preliminary, these findings suggest that the relationship between hippocampal anomalies and ADHD youth's susceptibility to developing depression and other mood disorders may merit further investigation with follow-up longitudinal research.

Psychol Rep. 2014 Apr;114:404-38.

**SEX DIFFERENCES AND THE INTERACTION OF AGE AND SLEEP ISSUES IN NEUROPSYCHOLOGICAL TESTING PERFORMANCE ACROSS THE LIFESPAN IN AN ADD/ADHD SAMPLE FROM THE YEARS 1989 TO 2009.**

**Fisher BC, Garges DM, Yoon SY, et al.**

Chart review of population (9 to 80 years) neuropsychological test battery for ADHD diagnosis, questionnaires with multiple responders were evaluated in outpatient setting from 1989-2009. The focus was gender differences across age, diagnostic group (ADHD-Inattentive/ADHD plus), neuropsychological test performance, and reported sleep symptoms over the lifespan. Individuals were assigned to ADHD-I group or ADHD plus group (based upon secondary diagnosis of sleep, behavioral, emotional disturbance); ADHD not primary was excluded (brain insult, psychosis). Among these were 1,828 children (ages 9 to 14), adolescents (ages 15 to 17), and adults (ages 18 and above); 446 children (312 diagnosed ADHD-I), 218 adolescents (163 diagnosed ADHD-I), and 1,163 adults (877 ADHD-I). Sleep was problematic regardless of age, ADHD subtype, and gender. The type and number of sleep problems and fatigue were age dependent. ADHD subtype, gender, fatigue, age, and sleep (sleep onset, unrefreshing sleep, sleep maintenance) were significant variables affecting neuropsychological test performance (sequencing, cognitive flexibility, slow- and fast-paced input, divided attention, whole brain functioning). Findings suggest that ADHD involves numerous factors and symptoms beyond attention, such as sleep which interacts differently dependent upon age.

Res Dev Disabil. 2014 May;35:1072-86.

**PSYCHIATRIC SYMPTOMS IN BOYS WITH FRAGILE X SYNDROME: A COMPARISON WITH NONSYNDROMIC AUTISM SPECTRUM DISORDER.**

**Thurman AJ, McDuffie A, Hagerman R, et al.**

In the present study, we examined the profile of psychiatric symptoms in boys with fragile X syndrome (FXS) using a parent report instrument. In addition, by comparing boys with FXS to boys with nonsyndromic autism spectrum disorder (ASD) utilizing multiple matching strategies, we examined between-group differences in the types of psychiatric symptoms observed and in the strength of their concurrent associations. Across all matching strategies, symptoms of manic/hyperactive behaviors and general anxiety were more frequently reported for boys with FXS than for boys with nonsyndromic ASD. Results also indicated a positive association between

social avoidance and general anxiety in FXS that was stronger than that observed in nonsyndromic ASD across all matching strategies. Theoretical and treatment implications are discussed.

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Res Dev Disabil. 2015;36:338-57.

**WHAT IS THE EVIDENCE OF IMPAIRED MOTOR SKILLS AND MOTOR CONTROL AMONG CHILDREN WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER (ADHD)? SYSTEMATIC REVIEW OF THE LITERATURE.**

**Kaiser M-L, Schoemaker MM, Albaret J-M, et al.**

This article presents a review of the studies that have analysed the motor skills of ADHD children without medication and the influence of medication on their motor skills. The following two questions guided the study: What is the evidence of impairment of motor skills and aspects of motor control among children with ADHD aged between 6 and 16 years? What are the effects of ADHD medication on motor skills and motor control? The following keywords were introduced in the main databases: attention disorder and/or ADHD, motor skills and/or handwriting, children, medication. Of the 45 articles retrieved, 30 described motor skills of children with ADHD and 15 articles analysed the influence of ADHD medication on motor skills and motor control. More than half of the children with ADHD have difficulties with gross and fine motor skills. The children with ADHD inattentive subtype seem to present more impairment of fine motor skills, slow reaction time, and online motor control during complex tasks. The proportion of children with ADHD who improved their motor skills to the normal range by using medication varied from 28% to 67% between studies. The children who still show motor deficit while on medication might meet the diagnostic criteria of developmental coordination disorder (DCD). It is important to assess motor skills among children with ADHD because of the risk of reduced participation in activities of daily living that require motor coordination and attention.

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Res Dev Disabil. 2015;36:384-95.

**IS THE IMPAIRMENT IN TEMPORAL ALLOCATION OF VISUAL ATTENTION IN CHILDREN WITH ADHD RELATED TO A DEVELOPMENTAL DELAY OR A STRUCTURAL COGNITIVE DEFICIT?**

**Donnadieu S, Berger C, Lallier M, et al.**

We investigated the temporal allocation of visual attention in 11-year-old children with attention-deficit/hyperactivity disorder (ADHD) by comparing their attentional blink (AB) parameters (duration, amplitude and minimum performance) with those observed in three groups of healthy control participants (8-year-olds, 11-year-olds and adults). The AB is a marker of impaired ability to detect a second target following the identification of a first target when both appear randomly within a rapid sequence of distractor items. Our results showed developmental effects; with age, the AB duration decreased and the AB minimum moved to shorter lag times. Importantly, 11-year old children with ADHD presented much the same similar AB patterns (in terms of duration and minimum position) as the healthy 8-year-old controls. Our results support the hypothesis whereby impaired allocation of temporal selective attention in children with ADHD is due to a developmental delay and not a specific cognitive deficit

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Res Dev Disabil. 2015;36:55-61.

**DEVELOPMENTAL LAG OF VISUOSPATIAL ATTENTION IN DUCHENNE MUSCULAR DYSTROPHY.**

**Piccini G, Gazzellini S, D'Amico A, et al.**

Children with Duchenne muscular dystrophy (DMD) present a specific deficit of voluntary attention but to date there has been no clear characterization of their attentional skills. The present study investigated the hypothesis that DMD patients present deficits of both voluntary and automatic visuospatial attention systems and that their performance could be equivalent to that of younger healthy males. Twenty males (mean age 10 years) with diagnosis of DMD, 20 age-matched healthy males (10 years 3 months) and 20 healthy younger males (7 years 6 months) were required to perform two visuospatial attention tasks: voluntary and automatic. In the voluntary task, the performance of the DMD group was significantly worse than that of the age-matched group, and equal to that

of the younger controls. In the automatic attention task also, the performance of the DMD patients was less efficient than that of the age-matched controls and equal to that of the younger children. This study supports the previous report of voluntary attention deficit in DMD and extends the evidence to include also an automatic attention system deficit. The development level of attention in DMD patients is below that expected for their age and corresponds to a delay of about three years.

Tidsskr Nor Laegeforen. 2014 Apr;134:689.

**CARDIOVASCULAR RISK IN ADHD TREATMENT IN CHILDREN.**

**Nilsen CV.**

Tijdschr Psychiatr. 2014;56:10-19.

**PREVALENCE, PERSISTENCY AND CONSEQUENCES OF ADHD IN THE DUTCH ADULT POPULATION.**

**Tuithof M, Ten HM, van DS, et al.**

**BACKGROUND:** Little is known about the prevalence and the consequences of attention-deficit hyperactivity disorder (ADHD) among adults in the general Dutch population.

**AIM:** To ascertain the prevalence of ADHD in childhood and adulthood, to investigate characteristics associated with the prevalence and persistency of ADHD and to draw a number of comparisons: to compare the functioning of adults with ADHD with that of people with a different mental disorder and to compare the extent to which these groups make use of treatment facilities.

**METHOD:** Data were derived from the Netherlands Mental Health Survey and Incidence Study-2 (NEMESIS-2), in which the occurrence of ADHD was determined in a representative sample of the Dutch population (n = 3,309; aged 18-44).

**RESULTS:** 2.9% of the respondents had had ADHD in childhood, 70.0% of them still had the disorder in adulthood. An anxiety disorder before the age of 16 increased the risk of ADHD persistency, whereas an impulse-control disorder decreased this risk. ADHD in adulthood was associated with lower socio-economic status, mental disorders, poor functioning and increased use of treatment facilities. ADHD adults and adults with an anxiety or substance use disorder showed very similar functional limitations and used treatment facilities to approximately the same extent.

**CONCLUSION:** More than two-thirds of the adults who had had childhood ADHD still had the disorder in adulthood. The consequences of this in terms of functioning and use of treatment facilities are substantial.

Tijdschr Psychiatr. 2014;56:162-66.

**DSM-5: NEURODEVELOPMENTAL DISORDERS.**

**Zinkstok J, Buitelaar J.**

**BACKGROUND:** The 5th edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM) was published in May, 2013.

**AIM:** To review the changes in the diagnostic criteria for autism spectrum disorder (ASD) and ADHD in DSM-5, compared to DSM-IV.

**METHOD:** The diagnostic criteria for ASD and ADHD in DSM-IV and DSM-5 are compared. The new diagnostic criteria are summarised and relevant literature is discussed.

**RESULTS:** The new category ASD includes the majority of the pervasive developmental disorders; however, in DSM-5, patients without stereotypical patterns of behaviour or interests will, from now on, be classified as having Social Communication Disorder. The threshold for meeting the diagnostic criteria for adhd has been lowered slightly. However, this is supported by clinical and epidemiological data and is unlikely to result in over-diagnosis.

**CONCLUSION:** Research into subtypes of asd may stagnate as a result of the changes introduced in DSM-5.

For clinicians, the diagnostic criteria for ASD and ADHD may be more clear-cut and possibly more user-friendly than the diagnostic criteria for these disorders as given in dsm-iv.

Value Health. 2014;17:A461.

**THE IMPACT ON WORK AND SOCIAL ACTIVITIES AMONG CARERS OF CHILDREN WITH ADHD IN SWEDEN RELATIVE TO OTHER NORDIC COUNTRIES.**

**Romero B, Gajria K, Dietrich CN, et al.**

**Objectives:** To understand social and work impacts of caring for children/ adolescents with attention-deficit/hyperactivity disorder (ADHD) in Sweden relative to a combined cohort of other Nordic countries (Denmark, Finland and Norway).

**Methods:** Carers in Sweden and other Nordic countries completed the Caregiver Perspective of Pediatric ADHD (CAPPA) online survey capturing carer impacts, including work, social activities and family relationships, due to their child's ADHD. Impacts were explored when the child was nullonnull and nulloffnull medication (e. g. days medication not taken). Comparisons of nullonnull and nulloffnull medication were examined using the Wilcoxon Signed-Rank test. No statistical comparisons of impacts were made between countries.

**Results:** 219 Swedish and 249 other Nordic carers of ADHD children aged 6-17 years completed the survey. 37% of Swedish carers reported employment changes (e. g. resigned, changed shift, reduced hours) due to their child's ADHD; 52% of these changes occurred when the child was nullonnull medication. In the past 4 weeks, 60% of Swedish carers reported missing work and 45% reported being late for work. After excluding outliers (n= 15), mean number of hours missed was 4.32 (n= 91, SD 2.53) and mean number of times late was 2.91 (n= 69, SD 1.35). Swedish carers reported fewer nullmoderatenull to nulltremendousnull impacts on social life when their child was nullonnull versus nulloffnull medication (partner relationship strain: 37% vs 67%; relationship strain with other children: 29% vs 57%; social activity interference: 40% vs 59%). Relative to other Nordic countries, more Swedish carers reported being late for work (36% vs 45%) and more nullmoderatenull to nulltremendousnull interference with social activities while the child was medicated (29% vs 40%). All other impacts described were similar between the two cohorts.

**Conclusions:** While medication helped, it did not completely alleviate child ADHD-related impacts on work and social activities among carers from Sweden and other Nordic countries.

Value Health. 2014;17:A454.

**SYSTEMATIC LITERATURE REVIEW AND MIXED TREATMENT COMPARISON OF GXR VERSUS OTHER TREATMENTS IN CHILDREN AND ADOLESCENTS WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER (ADHD).**

**Joseph A, Ayyagari R, Bischof M, et al.**

**Objectives:** This study compared the clinical efficacy of ADHD treatments in children and adolescents.

**Methods:** A systematic literature review was conducted, according to National Institute for Health and Care Excellence guidelines, to identify randomized controlled trials (RCTs) of guanfacine (GXR), atomoxetine (ATX), lisdexamfetamine (LDX), and methylphenidate (MPH) extended release (ER) and immediate release (IR) in children and adolescents with ADHD. A Bayesian mixed treatment comparison was conducted to compare baseline-to-endpoint change in ADHDRS- IV score, response (defined as a clinician global impressions - improvement [CGI-I] score (less-than or equal to) 2), with meta-regression adjustments permitted by data availability (age and percent female). 95% credible intervals (CrIs) for treatment effects and the posterior probability that GXR was more efficacious than each treatment were estimated.

**Results:** Of 5,619 records retrieved, 29 RCTs met the inclusion criteria. Five trials included GXR, 4 included LDX, 16 included ATX, 7 included MPH-ER, and 5 included MPH-IR. Per-arm patient sample size ranged from 29 to 222. The mean ADHD-RS-IV score change from baseline and 95% CrI (active minus placebo) were -8.68 (-10.63, -6.72) for GXR, -14.98 (-17.14, -12.80) for LDX, -6.88 (-8.22, -5.49) for ATX, and -9.33 (-11.63, -7.04) for MPH-ER. The relative risk and 95% CrI for CGI-I response (drug vs placebo) were 2.13 (1.68, 2.59) for GXR, 2.93 (2.47, 3.40) for LDX, 2.30 (1.79, 2.81) for MPH-ER, 1.97 (1.43, 2.58) for ATX, and 1.66 (1.02, 2.32) for

MPH-IR. Among non-stimulants, GXR was more effective than ATX when comparing ADHD-RS-IV change (with a posterior probability of 93.91%) and CGI-I response (posterior probability 71.01%).

**Conclusions:** This review found that LDX had greater efficacy compared with GXR, ATX, and MPH in the treatment of children and adolescents with ADHD with no overlap in Crls. Among non-stimulants, although GXR had a higher probability of being more efficacious than ATX, their Crls overlapped.

Value Health. 2014;17:A455.

#### OUTPATIENT TREATMENT OF ADOLESCENTS IN JAPAN WITH DRUGS FOR ATTENTION DEFICIT DISORDERS.

**Inagaki A, Nishimura Y, Otsuka H, et al.**

**Objectives:** To examine prescription patterns of drugs for the treatment of attention deficit disorders in Japanese children and adolescents.

**Methods:** We conducted a cross-sectional survey during October 2013 on outpatients aged 19 years or less in 34 private mental clinics. Patients who were prescribed at least one drug for the treatment of attention deficit disorders were analyzed in this report. Data were extracted on gender, age, principal psychiatric diagnosis (based on ICD-10), and types and doses of psychotropic drugs.

**Results:** The samples consisted of 286 males and 51 females. The average age (standard deviation) was 11.6 years (3.1). The mean length of psychiatric treatment was 21.3 months (24.0). The most frequent principal diagnostic category was nullbehavioral and emotional disorders with onset usually occurring in childhood and adolescencenull (F9; n= 237), followed by nulldisorders of psychological developmentnull (F8; n= 99), and nullmental retardationnull (F7; n= 1). Of 337 samples, 247 (73.2%) were prescribed OROS methylphenidate (OROS-MPH), a psycho-stimulant, while 141 (41.8%) received atomoxetine (ATMX), a selective noradrenalin reuptake inhibitor. OROS-MPH/ATMX combination therapy was administered to 51 (15.1%) of 337 patients. Antipsychotics were concurrently prescribed in 80 (23.7%) patients. Mood stabilizers were co-prescribed in 20 (5.9%) cases. Antidepressants were co-prescribed in 19 (5.6%) patients. Anxiolytics/hypnotics were concurrently prescribed in 13 (3.9%) patients.

**Conclusions:** In Japan, nearly one-sixth of the outpatients with attention deficit disorders received OROS-MPH/ATMX combination therapy.

Value Health. 2014;17:A462.

#### SOCIETAL COSTS AND QoL OF CHILDREN WITH ADHD AND THEIR PARENTS: A COMPARISON TO A REFERENCE GROUP FROM THE GENERAL POPULATION.

**Van Der Kolk A, Van AM, Bouwmans C, et al.**

**Objectives:** To compare Quality of Life (QoL) and societal costs in an ADHD population to a control group representing the general population.

**Methods:** An online cross-sectional retrospective study among parents of children with ADHD was conducted via Balans, a Dutch ADHD organization. Because of large differences in responder groups in the initial study, comparison with a control group was added to understand the impact of ADHD compared to the general population in greater detail. Therefore, a separate online research among parents of children without ADHD or any other chronic disease was performed. The control group was selected on the basis of pre-defined characteristics in order to match the ADHD group. QoL (EQ-5D for children and parents and KIDSCREEN-10 for children) and societal costs (TiC-P) were surveyed based on proxy reporting. In this study, monthly resource use of patients and their parents was identified. Descriptive statistics, independent samples t-test and Chi-square for p-values (sig. 2-tailed) were used for analysis on significance in differences between samples.

**Results:** The ADHD sample (n= 618) was compared to the control group (n= 704). Both groups primarily contained boys with a mean age of 11 years. QoL differed significantly between children with ADHD and the control group, both for EQ-5D (ADHD 0.80 vs. controls 0.96; p< 0.000) and KIDSCREEN-10 (ADHD 41.67 vs. controls 55.46; p< 0.000). The same is true for their parents (ADHD 0.83 vs. controls 0.88; p< 0.000). Total monthly costs associated with ADHD differed significantly as well, both for children (ADHD (euro) 518 vs. controls (euro) 91; p< 0.000) and parents (ADHD (euro) 288 vs. controls (euro) 49; p< 0.000).



**Conclusions:** Although this was not a direct comparative study, the magnitude of differences in absolute results seem to justify the conclusion that ADHD accounts for significantly higher costs and lower QoL for patients, parents and society compared to a control group representing the general population

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Z Kinder Jugendpsychiatr Psychother. 2014 Sep;42:337-47.

**GINKGO BILOBA EXTRACT EGb 761(R) IN CHILDREN WITH ADHD.**

**Uebel-Von SH, Rothenberger A, Albrecht B, et al.**

**OBJECTIVES:** The side effects, nonresponse, and prejudices against conventional pharmacological treatments call for complementary or alternative medical treatments (CAM) for ADHD. One possible treatment, at least for cognitive problems, might be the administration of Ginkgo biloba, though evidence is currently rare. This study tests the clinical efficacy of a Ginkgo biloba special extract (EGb 761(R)) and its correlation with brain electrical activity in children with ADHD combined type according to DSM-IV.

**METHOD:** In this open clinical pilot study, EGb 761(R) was administered to 20 children with ADHD over 3 to 5 weeks. Dosage was increased to a maximum of 240 mg daily if attention problems persisted. Possible drug side effects were assessed using the Side Effect Rating Scale. Efficacy was assessed in a multilevel approach including clinical assessment, quality of life (QoL), as well as performance and preparatory brain-electrical activity evoked during a Continuous Performance Test (Cue-CNV in the CPT).

**RESULTS:** A very low rate of mild adverse effects occurred during the observation period. Following EGb 761(R) administration, possible improvements in QoL, ADHD core symptoms as well as CPT performance were detected. Improved core symptoms were positively related to elevated CNV amplitude.

**CONCLUSION:** This preliminary evidence suggests that EGb 761(R) at a maximal dosage of 240 mg daily might be a clinically useful alternative treatment for children with ADHD, but further evidence is required before firm conclusions can be made.

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Z Kinder Jugendpsychiatr Psychother. 2014 Sep;42:325-35.

**EVALUATION OF THE MUSICAL CONCENTRATION TRAINING WITH PEPE (MUSIKO MIT PEPE) FOR CHILDREN WITH ATTENTION DEFICITS.**

**Rothmann K, Hillmer JM, Hosser D.**

**OBJECTIVE:** This study evaluates the Musical Concentration Training with Pepe ("MusiKo mit Pepe") for children aged 5 to 10 years with attention deficits.

**METHOD:** Using a pre-post-control design (N = 108), changes in attention capacity are measured by the Test of Attentional Performance for Children (KiTAP), whereas changes in the quality of life are assessed with the Children's Questionnaire (KINDL-R). Additionally, we utilized the Symptom Checklist for Attention Deficit Hyperactivity Disorders (FBB-ADHS) and for Conduct Disorder (FBB-SSV) of the Diagnostic System of Mental Disorders in Children and Adolescents II based on ICD-10 and DSM-IV as well as the Child Behavior Checklist and the Teacher's Report Form (CBCL, TRF).

**RESULTS:** Significant pre-post effects were found in both attention and quality of life for children treated by the training compared to controls. Moreover, significant reductions were detected in ADHD symptomatology in parents' and teachers' ratings, and in internal problems in parents' ratings. The effectiveness of the intervention was not affected by age, sex, intelligence, or migration background.

**CONCLUSION:** The music-based training "MusiKo mit Pepe" is an effective intervention for children with attention deficits, pending replication of these findings in future studies.

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Z Kinder Jugendpsychiatr Psychother. 2014 May;42:147-55.

#### **ASSOCIATIONS WITH ADHD AND PARENTAL DISTRESS WITH IN PLAY IN EARLY CHILDHOOD.**

**Weber-Borgmann I, Burdach S, Barchfeld P, et al.**

**OBJECTIVE:** According to Papousek (2004), "disinterests in play" in early childhood is a possible early indicator of AD(H)D at school age. The phenomenon of disinterest in play is associated with psychological distress in parents and children as well as with disturbances in the parent-child-relationships Papousek, 2003. We investigated the association between disinterest in play in early childhood and AD(H)D and their associations with maternal distress.

**METHOD:** Mothers of 35 children with AD(H)D [age: M (SD)= 9.0 (1.1) years; males: 30 (85.7 %)] and mothers of 42 children without AD(H)D [age: M (SD) = 8.8 (1.0) years; males: 35 (83.3 %)] gave their written informed consent to participate in the study. Using a questionnaire on the ability to play during the first 4 years of age, subjects were grouped into 39 children with lower interest in play and 38 children with higher interest in play. Maternal stress was assessed using a German adaptation of the Parenting Stress Index Abidin, 1995.

**RESULTS:** The rate of AD(H)D and maternal stress was significantly higher in the group of children with lower interest in play. Mothers of children showing both AD(H)D and lower interest in play scored highest, mothers of children presenting neither behavior disorder scored lowest.

**CONCLUSIONS:** The results agree with the assumption that disinterest in play in early childhood is associated with the development of AD(H)D and an additional stressor for mothers.

Zhonghua Er Ke Za Zhi. 2014 Apr;52:287-91.

#### **THERAPEUTIC EFFECTS OF EXERCISE-BASED TREATMENT PROGRAMME ON CHILDREN WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.**

**Zhang J, Wen F, Zhang J, et al.**

**OBJECTIVE:** To evaluate the effects of an exercise-based treatment programme (dyslexia, dyspraxia and attention-deficit treatment, DDAT) on various subtypes of attention-deficit/hyperactivity disorder (ADHD).

**METHOD:** Ninety-one ADHD children with standing balance dysfunction (ADHD-I 43, ADHD-HI 15 and ADHD-C 33) were given DDAT for 6 months, the efficacy of DDAT was evaluated before DDAT, three, six months after the treatment and three month after end of the treatment according to SNAP-IV, before and after the treatment by balancing function test and Conners Parents Rating Scale.

**RESULT:** Inattention subscale scores of ADHD-I, ADHD-HI and ADHD-C before and after the interventions were 1.99 +/- 0.34, 0.96 +/- 0.31, 2.17 +/- 0.31 and 1.19 +/- 0.45, 0.81 +/- 0.28, 1.32 +/- 0.37, differences of ADHD-I and ADHD-C were significant ( $P < 0.05$ ), hyperactivity subscale scores of three subtypes of ADHD were 0.81 +/- 0.35, 2.01 +/- 0.35, 1.96 +/- 0.33 vs. 0.45 +/- 0.33, 0.79 +/- 0.41, 1.10 +/- 0.35, there were significant differences as well ( $P < 0.05$ ). The score of hyperactivity symptom was reduced more compared to that of inattention symptom by the SNAP-IV scale parent forms. There were significant difference before and after the treatment based on Conners parent scale for conduct problem (1.11 +/- 0.48 vs. 0.76 +/- 0.44), learning problem (1.97 +/- 0.58 vs. 1.60 +/- 0.67), psychosomatic problems (0.61 +/- 0.49 vs. 0.29 +/- 0.35), activity/ hyperactivity (1.46 +/- 0.69 vs. 1.09 +/- 0.55) and anxiousness (1.05 +/- 0.63 vs. 0.62 +/- 0.47) as well ( $P < 0.05$ ); the standing balance dysfunction improved for most of the children, total effective rate was 87.9%, no significant difference was found among the three subtypes ( $P > 0.05$ ).

**CONCLUSION:** DDAT is a safe and efficient intervention for the ADHD children with standing balance dysfunction, the improvement on hyperactivity symptom was better than that on inattention symptom. This study shows that an exercise-based treatment programme for cerebellum function improves symptoms of ADHD and balance function.



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## Emotional reactivity in referred youth with disruptive behavior disorders: The role of the callous-unemotional traits



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## ABSTRACT

Deficits in emotional reactivity are frequently reported in Disruptive Behavior Disorders (DBDs). A deficit in prosocial emotions, namely the callous unemotional traits (CU), may be a mediator of emotional reactivity. Our aim is to investigate subjective emotional reactivity towards visual stimuli with different affective valence in youths with DBDs and healthy controls. The clinical sample included 62 youths with DBDs (51 males, 8 to 16 years, mean  $11.3 \pm 2.1$  years), the control group 53 subjects (36 males, 8 to 16 years, mean  $10.8 \pm 1.5$  years). The groups were compared using the Child Behavior Checklist (CBCL), the Inventory of Callous-Unemotional Traits (ICU), and the International Affective Picture System (IAPS), which explores the affective (pleasant/unpleasant emotional reaction) and arousal (low/high intensity of emotion) dimensions. The DBD group presented higher scores in externalizing and internalizing CBCL scores, and in ICU callous and indifferent subscales. At the IAPS, DBD patients differed from controls in the affective valence of the images, rating less unpleasant neutral and negative images. The CU traits were the only predictor of emotional reactivity in the DBD sample. A less aversive way to interpret neutral and negative stimuli may explain why DBD patients are less responsive to negative reinforcements.

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## 1. Introduction

Disruptive Behavior Disorders (DBDs), including Conduct Disorder (CD) and Oppositional Defiant Disorder (ODD), are among the most common reasons for youth referrals to mental health clinics (Steiner and Rensing, 2007) and can be associated with psychosocial impairment, poor prognosis and antisocial outcomes (Fergusson et al., 2005). A major goal in clinical research is to discover possible predictors of negative social outcome of DBDs, according to specific clinical, personality and temperamental variables on one side, and social and environmental variables on the other. These factors may allow further subtyping of the broad category of DBDs into more specific and homogeneous groups, improving intervention strategies (Mason et al., 2004; Vaughn et al., 2011). According to the recent DSM-5, DBDs are classified into a new cluster, named Disruptive, Impulse-control and Conduct disorders, including disorders

characterized by difficulties in emotional and behavioral self-control (American Psychiatric Association, 2013).

Among the clinical specifiers for a high-risk antisocial pattern, the DSM-5 has included limited pro-social emotions (Pardini et al., 2010; Burt et al., 2011). This proposed specifier is diagnosed if the patient meets full criteria for CD, and shows two or more of the following characteristics persistently over at least 12 months in more than one relationship setting: lack of remorse or guilt, callous-lack of empathy, unconcerned about performance, shallow or deficient affect. Individuals with callous-lack of empathy are cold and uncaring, and unconcerned about the feelings of others, even when their behavior results in harm to others. They do not express feelings and do not show emotions to others, or their emotions are insincere and used to manipulate others. These features were previously included in the concept of Callous Unemotional (CU) traits (Frick et al., 2003; Frick and White, 2008), and are also considered core elements in the clinical descriptions of adult psychopathy (Blair et al., 2006b). An additional feature of the CU traits is their stability from childhood to adolescence (Burke et al., 2007) and adulthood (Lynam et al., 2007). Previous research has

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shown that CU traits in childhood and adolescence have been related concurrently and prospectively with a higher rate of conduct problems (Rowe et al., 2010; López-Romero et al., 2011, 2012), aggressive behaviors (Marsee and Frick, 2007), and lower levels of pro-social behavior and social skills (Viding et al., 2009).

A significant body of research has been devoted to understanding temperamental and biological underpinnings of CU traits and psychopathy (Marsh et al., 2008; Viding et al., 2008, 2013; Jones et al., 2009), and also emotional reactivity to external stimuli has been explored in youth with high CU traits, as recently reviewed in Herpers et al. (2014). Children, adolescents and adults with psychopathic-like traits show some deficits in processing of negative emotional stimuli, or are less accurate in identifying sad facial expression (Kimonis et al., 2006; Woodworth and Waschbusch, 2008). A deficit in subjective arousal to fear and distress may lead youths to experience a lower impact of the negative consequences due to their own behaviors (Blair et al., 1997, 2001, 2006a, 2006b). The same emotional feature may also be associated with a reduced sensitivity to behavioral interventions (i.e., punishment) (Blair et al., 1997, 2001, 2006a, 2006b). A lower fear of social punishment may explain why youth with high CU traits are less responsive to treatment than peers with conduct problems, but low CU traits (Hawes and Dadds, 2005; Masi et al., 2013). A better understanding of the nature of CU traits can thus target more efficient treatment strategies specifically geared to the specific needs of the patients.

The International Affective Picture System (IAPS) is one of the most reliable and valid instruments for the experimental investigation of emotions based on a set of visual stimuli for the exploration of the relationships between the affective valence of the emotional stimuli (from pleasant to unpleasant), and the individuals' reaction in terms of arousal to emotional stimuli (from excited to calm) (Lang et al., 1999). Recently, IAPS has been applied to youths, based on norms by Lang et al. (1999). Early studies support the validity of IAPS for use in young samples from the community (McManis et al., 2001), as well its utility the exploration of psychopathic-like traits and conduct problems (Sharp et al., 2006, 2008). Following McManis et al. (2001) work with pre-adolescent children, words like happy, pleased, good, and unhappy, scared, angry, bad or sad were used in the instructions to describe the endpoints of the pleasure (valence) scales. Words like calm, relaxed, bored, or sleepy and excited, nervous or wide-awake described the endpoints for the arousal scale. Sharp et al. (2006) selected 27 IAPS pictures to explore a wide range of affective content in a large unselected community cohort of 659 children aged 7–11, while concurrent symptoms of DBDs and psychopathy were collected from multiple sources. According to this study, children above the cut-off on measures of antisocial behavior presented lower arousal to unpleasant picture, but higher arousal to pleasant picture.

A recent article by Herpers et al. (2014) reviewed the current literature on neurocognitive aspects of CU traits in youths. A lower emotional responsivity to distressing stimuli was found in the majority of studies, as well as a reduced response of the amygdala and a weaker connectivity between amygdala and the ventromedial prefrontal cortex, suggesting impaired emotional reactivity over and beyond conduct problems. These findings are in line with other studies, suggesting that specific emotion processing deficits, namely in the response to sad or fear stimuli, are related to changes in brain structure and function (Fairchild et al., 2013; Frick et al., 2014). These issues support the interest in using IAPS pictures in CD, as they comprise a various set of different emotions.

The current study on referred Italian children and adolescents with DBDs, is aimed at further exploring emotional reactivity associated with the presence of CU traits. Our hypothesis is that youth with DBDs that may show a different emotional subjective experience, evaluated on a self-report clinical scale, compared to healthy subjects. Based on previous neurobiological and psycho-

physiological studies (Patrick et al., 1993; Fowles, 2000; Van Goozen et al., 2007; De Wied et al., 2009), the presence of CU traits could be associated with reduced arousal and increased valence subjectively perceived against negative visual stimuli. The questions addressed in this study are therefore the following: 1) is there a specific pattern of emotional response, in terms of valence, arousal, or both in referred youth with DBDs, compared to healthy controls? 2) is there any relationship between arousal/valence facing emotional engaging stimuli and high level of CU traits?

## 2. Material and method

### 2.1. Participants

The clinical sample consisted of 62 children and adolescents with DBDs (ODD and/or CD), (51 males, age-range 8 to 16 years, mean age  $11.3 \pm 2.1$  years), consecutively referred to two third-level Italian departments of Child and Adolescent Psychiatry, settled in the Scientific Institute “Stella Maris” in Pisa and the Scientific Institute “Bambino Gesù” in Rome from January 2012 to February 2013. Our clinics are research hospitals with a national catchment for children and adolescents presenting a wide range of neuropsychiatric disorders. The children were referred by community-based child psychiatrists or pediatricians, or family members. All patients were diagnosed according to a systematic evaluation, including historical information, prolonged observation of interactions with peers, parents and/or examiners, and a structured clinical interview according DSM-IV criteria, the Schedule of Affective Disorders and Schizophrenia for School-Age Children - Present and Lifetime Version (K-SADS-PL) (Kaufman et al., 1997), administered by trained child psychiatrists. All the patients with current or past diagnosis of autism spectrum disorder, psychotic disorder, or with a Full Scale IQ below 75 according to Wechsler Intelligence Scale for Children-III (WISC-III), were excluded from the study. The control group consisted of 53 normal subjects (36 males, age-ranged 8 to 16 years, mean age  $10.8 \pm 1.5$ ). The clinical and the control groups did not differ according to both age and gender ratio (Table 1).

### 2.2. Procedures

The study design consisted in a multicenter, cross-sectional evaluation of children and adolescents, aged from 8 to 16 years, admitted to our clinics. The clinical sample was compared with a healthy control group, matched for age and gender ratio.

The control group was drawn from public elementary and junior high schools in the area of Pisa and Rome, all following regular education programs. The schools were selected randomly, and agreed to participate in the study. Handicapped children (i.e., intellectual disabilities, neurological disorders, autism spectrum disorders, or any other impairing condition identified during the school years) were excluded. After obtaining informed consent from school directors and teachers, the parents of the students were asked to complete the Italian version of Child Behavior Check List (CBCL) (Achenbach, 1991), and the participants were screened for behavioral and emotional problems.

All subjects participated voluntarily in the study after a written informed consent was obtained from parents or legal caregivers. The entire study protocol, which includes a wide range of neuropsychological tasks and psychopathological questionnaires, was approved by the Ethical Committee of both Hospitals.

### 2.3. Measures

Both the clinical and the control samples were assessed with the CBCL, a 118-item scale, completed by parents, which is one of the most frequently used instruments for epidemiological and clinical studies. Items are scored on a 3-step response scale, and grouped in 8 different syndromes (Withdrawn, Somatic Complaints, Anxious/Depressed, Social Problems, Thought Problems, Attention Problems, Delinquent Behavior and Aggressive Behavior). The CBCL provides a Total Problem Score, two broad-band scores designated as Internalizing Problems (including Withdrawn, Somatic Complaints and Anxious/Depressed syndromes) and Externalizing Problems (including Delinquent Behavior and Aggressive Behavior). CBCL inattention scale was more specifically considered, given the high ADHD comorbidity in the clinical sample.

The clinical sample was assessed with the K-SADS for the diagnosis of DBDs and comorbidities. The K-SADS was administered individually to the adolescents and their parents by trained child psychiatrists with specific experience in child and adolescent psychiatric disorders. To improve the reliability and validity of the diagnoses, after each interview, clinical data from each subject-parent pair were reviewed by the research clinicians for the purpose of consensus.

The Children's Global Assessment Scale (C-GAS) (Shaffer et al., 1983) was used to assess the functional impairment in both the clinical and control groups. The

Table 1

Comparison between the clinical group and the control group.

	Clinical group (N=62)		Control group (N=53)		F/ $\chi^2$ (d.f.)	p
<b>Males, n (%)</b>	51 (82)		36 (68)		2.5 (1)	0.117
<b>Mean age</b>	11.3 $\pm$ 2.1		10.8 $\pm$ 1.5		2.2 (113)	0.151
<b>Diagnosis (N, %)</b>						
Oppositional-defiant disorder	43 (68)		–			
Conduct disorder	19 (32)		–			
<b>Comorbidity (N,%)</b>						
ADHD	42 (67)	–	–	–	–	–
Mood disorders	5 (8)	–	–	–	–	–
Anxiety disorders	3 (5)	–	–	–	–	–
Obsessive-compulsive disorder	2 (3)	–	–	–	–	–
Enuresis	1 (1)	–	–	–	–	–
<b>Inventory of callous unemotional traits (Youth v.)</b>	Clinical group (N=62)		Control group (N=53)		F/ $\chi^2$ (d.f.)	p
Callous (mean, S.D.)	9.95	6.38	6.63	3.79	10.54 (113)	0.00**
Indifferent (mean, S.D.)	10.36	6.40	6.71	3.84	12.65 (113)	0.00**
Unemotional (mean, S.D.)	7.04	3.71	6.13	2.77	2.02 (113)	0.158
Total (mean, S.D.)	27.34	11.00	19.48	7.52	18.50 (113)	0.00**
<b>Child behavior checklist</b>	Clinical group (N=62)		Control group (N=53)		F/ $\chi^2$ (d.f.)	p
Tot. problems (mean, S.D.)	68.26	7.56	43.75	10.21	186.16 (113)	0.00**
Int. problems (mean, S.D.)	62.44	9.15	47.95	9.79	57.11 (113)	0.00**
Ext. problems (mean, S.D.)	67.96	8.64	44.32	8.13	191.32 (113)	0.00**
Anxiety problems (mean, S.D.)	62.70	8.70	53.45	5.13	37.82 (113)	0.00**
Withdrawal (mean, S.D.)	61.80	8.74	53.66	5.13	29.72 (113)	0.00**
Somatic complaints (mean, S.D.)	58.76	8.08	53.36	4.29	15.93 (113)	0.00**
Social problems (mean, S.D.)	64.72	8.28	52.73	3.85	78.43 (113)	0.00**
Thought problems (mean, S.D.)	62.94	9.52	51.59	3.29	56.91 (113)	0.00**
Breaking rules (mean, S.D.)	65.37	8.60	51.02	1.58	118.90 (113)	0.00**
Attention problems (mean, S.D.)	69.81	8.71	52.20	2.72	166.42 (113)	0.00**
Rule breaking (mean, S.D.)	65.37	8.60	51.02	1.58	118.90 (113)	0.00**
Aggressive behavior (mean, S.D.)	69.61	10.43	51.93	3.17	117.30 (113)	0.00**
C-GAS (mean, S.D.)	42.05	9.84	89.73	0.9	254.00 (113)	0.00**

C-GAS: Children- Global Assessment Scale; \*  $p < 0.05$ .\*\*  $p < 0.001$ .

C-GAS is a widely used, clinician rated measure describing the severity of functional impairment on a scale from 0 (severe impairment) to 100 (superior functioning). It was designed for use with children from 4 to 16 years of age; scores above 70 indicate normal functioning.

After the diagnostic and screening procedures, all participants were assessed with the following measures:

International Affective Picture System (IAPS), a set of visual stimuli for use in experimental investigations of emotion and attention (Lang et al., 1999). According to McManis et al. (2001), 60 images were selected from the IAPS full set (over 700 photographs), 20 pictures with pleasant images (for example, babies or young lovers), 20 pictures with unpleasant images (for example, snakes, violent death or weapons), and 20 neutral pictures (everyday objects) (see footnote for details)<sup>a</sup>. Data were collected using Self-Assessment Manikin (SAM) (Lang et al., 1999), an affective rating-scale system based on a graphical figure that depicts the dimensions of arousal (from an excited to a relaxed figure) and valence (from a smiling to a frowning figure) on a 9-point visual analog scale. Previous studies support the SAM as a valid instrument for dimensional ratings of valence and arousal in children and adolescents (Sharp et al., 2006). Regarding valence, low scores were indicative of unpleasant emotional reaction, and high scores were indicative of pleasant reactions. For arousal, low scores were indicative of low intensity of emotion, and high scores of strong emotional activation. The IAPS colored images were shown as slides using an electronic device, throughout an experimental package created on the Superlab psychological software version 4.1, occupying the entire screen, in a well lit room. Images were set in a fixed random sequence (the same for all participants). Each slide was presented for 6 s, followed by a blank screen for 6 s. Pressing the space bar, the subject advanced to the next slide. Subjects were asked to evaluate arousal and valence for each image, using the SAM, with the supervision of a child psychiatrist or a clinical psychologist. After the experiment, subjects were questioned on the content of some of the images, to confirm that they had fully attended to the stimuli. After subjects completed the task, they were rewarded with a certificate of completion and a small gift (a small toy).

<sup>a</sup> The following pictures from the IAPS were used: 1040, 1120, 1280, 1300, 1710, 1750, 1920, 1930, 2070, 2120, 2130, 2190, 2280, 2320, 2650, 2660, 2780, 2810, 2890, 2920, 3230, 3280, 3500, 3530, 5020, 5030, 5450, 5480, 5910, 5950, 6230, 6300, 6370, 7000, 7010, 7030, 7040, 7080, 7090, 7100, 7130, 7150, 7170, 7250, 7330, 7380, 7390, 7400, 7410, 7430, 7510, 8260, 8490, 8510, 8620, 9050, 9421, 9450, 9461, 9480.

Inventory of Callous-Unemotional Traits (ICU) (Frick, 2004), is a 24-item self-report questionnaire, completed by the children or adolescents, designed to assess the CU traits in three dimensions: callousness, indifferent, unemotional. Answers are recorded on four-point Likert scale. The ICU has been previously used in children aged 8 years or more (Muñoz, 2009; Feilhauer et al., 2012, 2013), and has been shown to be a reliable measure in children and adolescents (Kimonis et al., 2008; Feilhauer et al., 2013). The reliability of the ICU scores across studies has been proven to be acceptable (Neal and Sellbom, 2012).

#### 2.4. Statistical analysis

All analysis were performed using SPSS 9 for Windows. Chi square and one way analysis of variance (ANOVA) were used for categorical and continuous demographic variables. After controlling for normal distribution of variables, to test the group differences on IAPS scores, one-way ANOVA between groups were performed. For all tests, significance was set at  $p < 0.05$ . To test the relationship between CU traits and IAPS scores in the clinical group, six hierarchical multiple regressions were conducted, examining CU trait as predictors of scores on the IAPS dimension (valence/positive, arousal/positive, valence/neutral, arousal/neutral, valence/negative, arousal/negative). In all regression models, age and gender (demographic covariates) were entered at step 1, CBCL inattention symptoms and C-GAS clinical impairment (clinical covariates, selected because of the high ADHD comorbidity and functional impairment of the clinical sample) were entered at step 2, and CU main effects (assessed with the ICU subscales) were entered at step 3.

### 3. Results

#### 3.1. Comparison between groups according to CBCL and ICU

As expected, significant group differences resulted in all total scores and subscales (both externalizing and internalizing) at CBCL, as well as ICU callous and indifferent subscales. ICU unemotional subscale did not differ between clinical and control groups (Table 1).



### 3.2. Comparisons between groups according to IAPS

In the valence dimension, a group difference was found for neutral ( $F=11.46$ ,  $d.f.=113$ ,  $p=0.01$ ) and negative images ( $F=16.6$ ,  $d.f.=113$ ,  $p<0.001$ ), but not for positive stimuli ( $F=0.33$ ,  $d.f.=113$ ,  $p=0.565$ ). No group difference was found in evaluating positive ( $F=0.40$ ,  $d.f.=113$ ,  $p=0.527$ ), neutral ( $F=0.47$ ,  $d.f.=113$ ,  $p=0.49$ ) and negative ( $F=1.3$ ,  $d.f.=113$ ,  $p=0.24$ ) images for the arousal dimension. In summary, the children in clinical sample, when faced with neutral and negative set of stimuli, tended to evaluate them as less unpleasant, compared with the control sample. Data are summarized in Table 2.

### 3.3. Multiple regression analysis

Multiple regression analysis was performed on the clinical group for each dimension of IAPS score as the dependant variable. Results of regression analysis predicting IAPS negative valence score show that  $R^2$  accounts for 26% of variance at step 3. Relatively to the predictors in the full model at step 3, ICU-callousness ( $B=0.355$ ,  $p<0.01$ ) and ICU-unemotional ( $B=0.231$ ,  $p<0.05$ ) accounted independently for significant proportions of the variance. Thus, the callousness and unemotional dimensions of CU-traits resulted to predict a pleasant judgement to negative images.

Results of regression analysis predicting IAPS neutral valence score show that  $R$  differed significantly from zero at step 1 ( $R^2=0.170$ ), and improved model fit at step 3 ( $R^2=0.309$ ). Regarding the predictors in the full model at step 3, age ( $B=-0.379$ ,  $p<0.01$ ) and ICU-unemotional ( $B=0.358$ ,  $p<0.01$ ) independently accounted for significant proportions of variance. Thus, the unemotional dimension of CU-traits predicts a pleasant judgement to neutral images.

Results of regression analysis predicting IAPS negative arousal/calm score, IAPS neutral arousal/calm score, IAPS positive arousal/calm score and IAPS positive valence score show a lack of improvement model fit at all three steps. Data are shown in Table 3.

In summary, multiple regression analyses indicate that the distorted emotional processing in DBDs are related to the CU traits, but not to age, gender, ADHD inattentive symptoms and functional impairment.

## 4. Discussion

In present paper, we aimed at further exploring emotional reactivity in a sample of DBDs youths, and its possible relationship with CU traits. In this study we used well validated self-report measures, such as IAPS and ICU. Scheepers et al. (2011) pointed out the importance of self-reports for the assessment of CU traits in youth, as it is related to interpersonal thoughts and feelings, which may be hardly recognized and reported by parents.

Consistently with the existing literature (Frick et al., 2013; Herpers et al., 2014), we have found a distorted emotional reactivity in DBDs group, associated to higher CU traits. According to the IAPS, patients with DBDs differed from controls in the affective valence of the images, that is the degree of pleasure/ happiness or displeasure/sadness experienced by the subjects observing the emotional pictures, while no differences between groups were found for the self-reported arousal dimension, that is the excitement or activation degree produced by emotional images. Our patients rated both neutral and negative images as less unpleasant, whereas they did not differ from healthy controls in evaluating the positive images. In other words, images belonging to negative or neutral categories are less aversive for DBDs patients than for controls. Furthermore, the multiple regression analyses showed that the callousness and unemotional dimensions of CU-traits predict a non-negative judgement to negative images. This

**Table 2**

Mean and standard deviations of valence and arousal ratings at positive, neutral and negative images of International Affective Picture System (IAPS).

	Clinical group (N=62)		Control group (N=53)		Anova	
	Mean	S.D.	Mean	S.D.	F (d.f.)	p
<b>Positive</b>						
Valence ratings (H/U)	7.56	1.12	7.60	0.85	0.332 (113)	0.565
Arousal ratings (A/C)	2.97	1.35	2.80	1.40	0.402 (113)	0.527
<b>Neutral</b>						
Valence ratings (H/U)	5.70	1.03	5.12	0.74	11.463 (113)	0.01*
Arousal ratings (A/C)	3.74	1.24	3.57	1.26	0.479 (113)	0.490
<b>Negative</b>						
Valence ratings (H/U)	3.75	1.63	2.65	1.18	16.663 (113)	0.00**
Arousal ratings (A/C)	6.13	1.75	6.50	0.22	1.349 (113)	0.248

\*  $p<0.05$ .

\*\*  $p<0.001$ .

issue may help to understand why some DBDs patients are less responsive to negative reinforcements and punishments, and consequently more resistant to treatments (Van Bokhoven et al., 2005; Hawes and Dadds, 2005; Sharp et al., 2006; Masi et al., 2011; Kumsta et al., 2012). This may be relevant for treatment programs, such as psychotherapy and psycho-educational rehabilitation, and it may be a specific target of these interventions. It might be true that improvement of subjective emotional reactivity may improve prosocial behaviors, and overall prognosis. Our findings provide further support that an emotion recognition training (ERT) in early phase of conduct problems may improve several outcomes (such as affective empathy and behavior), as recently pointed out by Dadds et al. (2012). According to these authors, children with high CU traits responded less well to a treatment-as-usual, while ERT produced significant improvements in affective empathy and conduct problems in these children, regardless of their diagnostic status.

Of note, no differences between groups have been found for the self-reported arousal dimension, suggesting that patients with DBDs do not have an increased emotional activity facing both positive or negative stimuli. A different pattern has been found in (adult) patients with borderline personality disorder (BPD), who present a similar pattern of affective valence (images belonging to negative or neutral categories are less aversive than for controls, while no difference are found for pleasant images), but an increased arousal and more activation than controls (Jayaro et al., 2011). This finding further contributes to define specific emotional and behavioral features of DBDs, compared to BPD, although phenomenological similarities, as well as longitudinal association, has been reported (Belsky et al., 2012; Burke and Stepp, 2012). This is consistent with psychobiological models, showing that subjects with high CU traits present under-arousal, particularly facing negative stimuli and distress cues, according to several measures, such as heart rate, skin conductance and blood pressure (Blair et al., 1997).

A dissociation between self-reported responses and psychophysiological reactions to negative IAPS stimuli in adult and adolescents with psychopathic traits has been previously reported by Patrick et al. (1993) and Blair (1999). Previous studies have also found a significant relationship between self-reported subjective under-arousal and antisocial measures assessed by parents and teachers (Sharp et al., 2006; Michonski and Sharp, 2010). It may be hypothesized that the psycho-biological subjective under-arousal of youths with high CU traits may affect the subjective feelings of emotional states, such as excitation, distress and arousal, which are reported differently from normal youths. As hypothesized by Jayaro et al. (2011) for BPD patients, further studies should determine whether patients with DBDs may respond differently



**Table 3**  
Summary of hierarchical regression analyses predicting International Affective Picture System scores ( $N=62$ ).

DV	Predictor	Model 1				Model 2				Model 3			
		$R^2$	$\Delta R^2$	$F$	$\beta$	$R^2$	$\Delta R^2$	$F$	$\beta$	$R^2$	$\Delta R^2$	$F$	$\beta$
Neg. valence		0.044	0.011	0.348		0.045	–0.023	0.664		0.265*	0.169*	2.775*	
	Gender				–0.177				–0.182				–0.193
	Age				0.117				0.118				0.075
	C-GAS								0.029				0.082
	CBCL-A								0.003				–0.016
	ICU-CAL												0.355**
	ICU-IND												0.025
Neg. arousal		0.034	0.001	1.030		0.040	–0.028	0.591		0.173	0.066	1.613	0.231*
	Gender				0.088				0.065				0.080
	Age				–0.164				–0.162				–0.068
	C-GAS								0.002				–0.052
	CBCL-A								0.082				0.137
	ICU-CAL												–0.203
	ICU-IND												–0.235
Neu. valence		0.170**	0.142**	6.047**		0.201*	0.145*	3.583*		0.308**	0.220**	3.455**	–0.141
	Gender				–0.152				–0.089				–0.082
	Age				–0.379**				–0.386**				–0.414**
	C-GAS								–0.106				–0.049
	CBCL-A								–0.166				–0.153
	ICU-CAL												–0.057
	ICU-IND												–0.057
Neu. arousal		0.013	–0.020	0.397		0.025	–0.044	0.361		0.128	0.015	1.133	0.358**
	Gender				–0.002				–0.009				0.005
	Age				–0.115				–0.117				–0.011
	C-GAS								–0.079				–0.131
	CBCL-A								0.064				0.124
	ICU-CAL												–0.059
	ICU-IND												–0.288*
Pos. valence		0.046	0.014	1.434		0.050	–0.017	0.743		0.148	0.038	1.343	–0.116
	Gender				–0.138				–0.149				–0.131
	Age				–0.161				–0.158				–0.064
	C-GAS								0.058				0.043
	CBCL-A								0.010				0.082
	ICU-CAL												–0.078
	ICU-IND												–0.349*
Pos. arousal		0.017	–0.017	0.502		0.102	0.039	1.627		0.159	0.050	1.456	0.124
	Gender				–0.068				0.031				0.032
	Age				–0.108				–0.122				–0.060
	C-GAS								–0.231				–0.275*
	CBCL-A								–0.234				–0.212
	ICU-CAL												0.093
	ICU-IND												–0.126
	ICU-UNE												–0.185

C-GAS: Children's Global Assessment Scale; CBCL-A: Child Behavior Checklist, Attention problems; ICU-CAL: Inventory of Callous-Unemotional Traits, Callous; ICU-IND: Inventory of Callous-Unemotional Traits, Indifferent; ICU-UNE: Inventory of Callous-Unemotional Traits, Unemotional.

\*  $p < 0.05$ .

\*\*  $p < 0.01$ .

to different kinds of unpleasant pictures, such as those including a more evident social dimension (Sloan et al., 2010).

Our patients with DBDs presented higher scores in all the CBCL scales. Although it might be expected that the clinical sample presents more severe symptoms in the externalizing domain compared to the control group, as well as in CU traits, it is relevant that all the internalizing syndrome scores were higher as well, as high internalizing scores are not fully consistent with high CU features. It may be hypothesized that our patients, recruited from a psychiatric cohort, present a specific quality of emotional dysregulation, consisting of a complex combination of both callousness, and anxiety/depression, with low self-awareness and uncommon help-seeking behavior. This association may represent a meaningful feature in youths with DBDs. It should also be noted that the CBCL questionnaire was scored by the parents who, gave the

impact of disruptive behaviors, may have overestimated the psychopathological meaning of their children's behaviors.

A limitation of our study is its cross-sectional design. An important issue to further explore is the stability of the emotional reactivity over time, particularly from childhood to adulthood, both in referred and in healthy youths. A second limitation is the wide age range of both samples, although no age effect emerged, except for one regression model (neutral valence). We found that valence ratings to neutral pictures decrease with age, whereas, contrary to findings of Sharp et al. (2006), the age does not affect the arousal ratings. This developmental component is intriguing and could be an interesting aim for future research works. Third, the high prevalence of males is an unavoidable limit, considering the epidemiology of DBDs; however, no gender effect emerged from analysis. However, the gender effect on emotional reactivity

on youths with DBDs needs to be further explored with specific study design addressing possible specificities. For example, elevated CU traits in girls may have been associated with different comorbidity patterns (i.e. in anxiety disorders), compared to boys.

In summary, we propose that emotional dysregulation is a central psychopathological issue in youths with DBDs, and this characteristic should be carefully considered in the assessment of these patients. The literature on this kind of emotional dysregulation in the presence of CU traits is still sparse and (much) more research is needed in this field. The improvement of emotional reactivity may become an important goal of the treatment procedure, and it may be associated with enhanced improvements even on conduct problems, in terms of intensity and stability over time.

### Conflict of interest

Dr. Masi was in the advisory boards for Eli Lilly and Shire, has received research grants from Eli Lilly and Shire, and has been speaker for Eli Lilly, Shire, Lundbeck, Otsuka and Novartis. Dr. Vicari was in the advisory boards for Shire, has received research grants from Eli Lilly and Shire, and has been speaker for Eli Lilly, Shire. Dr. Mazzone has received travel grant from Shire and has been speaker for Eli Lilly. All the other authors do not have conflicts of interest to declare.

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## Research in Developmental Disabilities



## Developmental lag of visuospatial attention in Duchenne muscular dystrophy



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## ABSTRACT

Children with Duchenne muscular dystrophy (DMD) present a specific deficit of voluntary attention but to date there has been no clear characterization of their attentional skills. The present study investigated the hypothesis that DMD patients present deficits of both voluntary and automatic visuospatial attention systems and that their performance could be equivalent to that of younger healthy males. Twenty males (mean age 10 years) with diagnosis of DMD, 20 age-matched healthy males (10 years 3 months) and 20 healthy younger males (7 years 6 months) were required to perform two visuospatial attention tasks: voluntary and automatic. In the voluntary task, the performance of the DMD group was significantly worse than that of the age-matched group, and equal to that of the younger controls. In the automatic attention task also, the performance of the DMD patients was less efficient than that of the age-matched controls and equal to that of the younger children. This study supports the previous report of voluntary attention deficit in DMD and extends the evidence to include also an automatic attention system deficit. The development level of attention in DMD patients is below that expected for their age and corresponds to a delay of about three years.

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## 1. Introduction

Duchenne muscular dystrophy (DMD) is a neuromuscular disease which has a major impact on the lives of the affected individuals, their families, and society. This genetic pathology affects one in every 5000 newborn males and is inherited in an X-linked recessive pattern (Blake & Kröger, 2000; Mehler, 2000; Miller & Wessel, 1993). The mutation process of the Xp21 (or DMD) gene, which encodes a protein called dystrophin, produces muscle weakness and physical limitations associated with cognitive and neuropsychological deficits (Wicksell, Kihlgren, Melin & Eeg-Oloffson, 2004). The latter are not progressive, unlike the muscular symptoms.

Dystrophin is found mainly in the muscle fibers, but occurs also in other organs such as the brain and the retina. This protein is expressed during several specific isoforms, some exclusive, others predominant in the brain (Lidov, 2000).

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Ricotti, Roberts, and Muntoni (2011) suggested that dystrophin plays a role in GABAergic synapses, critical in cognitive functions. Consequently, cognitive assessments carried out in DMD individuals showed impairment in executive functions, attention and verbal memory (Cotton, Voudouris & Greenwood, 2000; Marini et al., 2007; Mento, Tarantino & Bisiacchi, 2011; Poysky, 2007). Several studies in the last decades confirmed that individuals affected by DMD may present compromised cognitive development. The Intellectual Quotient (IQ) of Duchenne patients is normally one standard deviation below the average for the general population (Cotton et al., 2000). Moreover, the result of genotype-phenotype correlation in DMD showed that individuals with mutations affecting all the isoforms (downstream of exon 63) usually presented an intellectual disability. Conversely, individuals with mutations affecting only full-length isoforms (upstream of exon 30) less frequently presented intellectual disability (Ricotti et al., 2011).

Recently, higher rates (11–33%) of comorbid disorders, including attention-deficit-hyperactivity (ADHD), have been reported in Duchenne patients (Hendriksen & Vles, 2008; Pane et al., 2012; Steele et al., 2008). Despite growing interest in this comorbidity, few systematic studies have been carried out. Most of these investigations used parental questionnaires or surveys in their methodology, while in other studies attention deficit was evidenced using neuropsychological tasks (Cotton, Crowe & Voudouris, 1998; Hinton, De Vivo & Nereo, 2000). However, the presence of attention impairment in DMD is still controversial owing to the small number of studies, some of which excluded attention dysfunction (Hinton et al., 2000; Mento et al., 2011).

Dystrophin is concentrated in the postsynaptic pyramidal cells of the cerebral cortex (especially in the deep layers of the frontal cortex), in the hippocampus and in the soma and dendrites of Purkinje cells in the cerebellum. Therefore, dystrophin is mainly expressed in the frontal networks involved in attention orienting. In fact, fMRI studies in healthy individuals showed that a dorsal fronto-parietal network is active during top-down attention control, which is voluntary driven by semantic information (endogenous stimulus). A second network, made up of ventral fronto-temporo-parietal areas seems to be modulated by the detection of unexpected or peripheral events (exogenous stimuli) which automatically capture our attention (Corbetta & Shulman, 2002; Corbetta, Kincade, Ollinger, McAvoy & Shulman, 2000; Corbetta, 1998; Perry & Zeki, 2000).

The only study in which an experimental manipulation of attention has been carried out in patients with DMD is that of De Moura, Do Valle, Resende, and Pinto (2009). They used two Posner type tasks to evaluate voluntary and automatic visual orienting of attention with minimum working memory involvement. In the Posner paradigm, the participants respond to a target stimulus as quickly as possible. In the valid condition, the locus of target appearance is anticipated by a visual cue. In the invalid condition, however, the cue does not indicate the position of the target which will follow (Posner & Mitchell, 1967; Posner, 1980). In the automatic attention task, the cue is peripheral to the fixation point and automatically captures the attentional focus (exogenous stimulus). In the voluntary attention task, the cue appears in a central position and requires semantic processing (endogenous stimulus).

From the analysis of reaction times (RTs) obtained by De Moura et al. (2009) it emerged that patients with DMD present significantly increased attentional costs and benefits compared to the control group only in the voluntary attention task. DMD patients also showed a larger error rate in the invalid condition. Moreover, on the basis of previous studies on attentional control conducted in samples of children with typical development (Perchet & Garcia-Larrea, 2005; Wetzel & Schröger, 2007), De Moura and colleagues hypothesized that their 12-year-old DMD subjects would perform similarly to a group of 6–9-year-old children with typical development. However the authors did not directly verify this hypothesis.

De Moura et al. (2009) considered their results as evidence of voluntary, but not automatic, attention deficit in DMD. However, careful observation of the data reveals significantly longer reaction times (RTs) of DMD compared to controls (about 375 ms vs. 310 ms respectively) in the automatic orienting of attention task (valid condition). This result is therefore consistent with difficulties even in the automatic attention system.

The authors stated that longer raw RTs are just a sign of a motor deficit of the DMD group. However, similar mean RTs of the two groups (about 320 ms vs. 325 ms) were observed in the “valid condition” of the voluntary attention task, where the cue is effectively informative of the target position (less cognitively demanding condition). This result would indicate that the cognitive processing of the stimuli, more than the motor deficit, is responsible for the RT delay.

The main goal of this research is to investigate attentional skills in subjects impacted by the absence of full-length dystrophin expression, as occurs in DMD. In particular, we hypothesize that patients with DMD present deficits of both voluntary and automatic visuospatial attention orienting systems. Moreover, the present study aims to test the hypothesis concerning DMD's developmental delay of attentional skills. We hypothesize a worse performance in attentional tasks of DMDs compared to an age-matched control group, but a similar performance compared to a younger control group (i.e., three years younger).

We used one voluntary and one automatic orienting of attention task (Posner paradigm) which were modified ad hoc with respect to those by De Moura and colleagues. Responses in our tasks were made by just pressing the spacebar (instead of two possible response buttons as in the previous study) and target stimuli were presented in four possible positions arranged in the shape of a cross (instead of two horizontal positions). The rationale of these choices was that we wanted to minimize the bias due to the motor component of response production, given the involvement of dystrophin in motor control and the recruitment of a young control group, and also to be sure that the attentional focus was shifted not only horizontally, but on the whole perceptive field. We used an additional neutral condition, ‘no-cue trials’, to observe the ability of reaction to unexpected stimuli (vigilance), in both the automatic and voluntary attention task. Three groups: patients with DMD, age-matched healthy controls and younger healthy controls, performed the two attention tasks.

## 2. Methods

### 2.1. Participants

Twenty children with a mean age of 10 years (range: 8 years, 2 months–13 years, 1 months) affected by Duchenne Muscular Dystrophy participated in the study (DMD group). The inclusion criteria were the presence of the genetic diagnosis of Duchenne muscular dystrophy, unimpaired functionality of the upper limbs distal level evaluated with the *Performance of the Upper Limb* (PUL; raw scores below 1.5 standard deviation from the average), a specific scale for assessing upper limb in DMD patients (Mayhew et al., 2013) and an IQ in the normal range ( $IQ \geq 80$ ). All patients were followed up at the neurology unit of the Bambino Gesù Children's Hospital in Rome.

Forty healthy children with negative histories of neurological, psychiatric, tumoral, progressive metabolic and identified genetic pathologies, were also recruited from the schools of the “Bambino Gesù” Children's Hospital's neighborhood. They were divided into two control groups of 20 participants. The first control group (age-matched) was matched for chronological age (mean 10 years, 3 months; range 8 years, 4 months–13 years, 3 months), socio-economic status and level of education with the DMD group. The second control group (younger 6–9) was selected on the basis of a lower chronological age (mean: 7 years, 6 months; range: 6 years, 4 months–9 years, 1 months) but same socio-economic status compared to DMDs.

All the participants had normal or corrected vision and a normal non-verbal IQ measured with Raven's CPM (Belacchi, Scalisi, Cannoni & Cornoldi, 2008). Non-verbal IQ was preferred, since the tasks the participants were required to perform were non-verbal. The IQs of the DMD group, the control group with same chronological age, and the control group of 6–9 years were 105 ( $\pm 15$  SD), 112 ( $\pm 11$  SD) and 110 ( $\pm 13$  SD) respectively ( $p > .05$  for both comparisons). All the children were attending elementary or middle schools at the time of participation in the experiments.

All the participants and their parents gave informed consent before starting the experimental sessions. The procedure was approved by the Ethics Committee of “Bambino Gesù” Children's Hospital.

### 2.2. Procedures

Participants were tested individually in a dimly lit room. They stayed 40 cm in front of a computer screen with dark-gray background and luminance equal to 3 cd/m<sup>2</sup> on which the experimental stimuli appeared. The experiment consisted of two tasks: an automatic and a voluntary attention task.

The automatic visuospatial attention task included a block of 112 trials. Each trial began with a cross (fixation point) displayed in the middle of the screen for 1500 ms, followed by a sound alert for 300 ms (Fig. 1). Four empty squares (side 1.5 cm, 7.5 cd/m<sup>2</sup>, centered at 8.1 degrees of visual angle from the fixation point) were placed on the left, right, above and below the fixation point, and remained visible for 300 ms. After that, the border of one of the four squares blinked (luminance flash of 33 cd/m<sup>2</sup>) inducing automatic orienting of attention (20% of trials of blinking of each square). A variable interstimulus trial interval (ISI) was selected: 65 ms in 50% of cases and 115 ms in the remaining 50% of cases. After 35 ms, the target stimulus, represented by a white circle (6 cd/m<sup>2</sup>, centered at 8.2 degrees of visual angle from the fixation point), was presented in one square for a duration of 50 ms.

In the ‘valid’ condition, the cue correctly indicated the position of the upcoming target. In the ‘invalid’ condition the target did not appear in the blinking square but in a non-blinking one. Finally, in the ‘neutral’ condition the appearance of the target was preceded by the blinking of all four squares. In the ‘neutral no-cue’ condition no cue (no blinking square) preceded the target. The trials were 36% ‘valid’ trials, 36% ‘invalid’, 11% ‘neutral’ and 11% ‘neutral no-cue’ trials. The trials were combined randomly within each experimental run. Subjects were asked to detect and respond to a visual stimulus (the target) as quickly as possible by pressing the space bar with both hands.

The voluntary visuospatial attention task included 112 trials. After the appearance on the screen of a fixation point and a sound alert, four squares remained visible for 300 ms (side 1 cm, luminance 30 cd/m<sup>2</sup>, centered at 2.6 degrees of visual angle from the fixation point). Subsequently a cue appeared, represented by the singleton (red) on one of the squares for 50 ms, while the remaining three were green. The variable ISI was 800 ms in 46% of cases, 1000 ms in 46% of cases, and 500 ms, 600 ms and 700 ms in 3% each of cases. Trials characterized by the last three ISI have been used as a catch trial and were not included in the statistical analysis. A white dot (10 cd/m<sup>2</sup>), the target stimulus, subsequently appeared for 50 ms in one of the squares. The experiment consisted of 57% ‘valid’ trial, 21% ‘invalid’ trial, 11% ‘neutral no-cue’ and 11% ‘neutral’ trials. The participants were instructed to stare at the fixation point without moving their eyes, and to press the spacebar as fast as possible (with both hands) when the target stimulus appeared.

The software E-Prime 2.0 was used for the visual presentation of the stimuli and data collection. The timing accuracy of the software is  $\pm 0.5$  ms.

### 2.3. Statistical analysis

Weighted RTs, i.e., RT divided by the number of the correct responses for each condition of the task, were measured in the different trial types (as dependent variable). Weighted RT is a dependent variable usually employed in the literature on attention and which takes into account simultaneously both RTs and percentage of error. RTs were analyzed using a



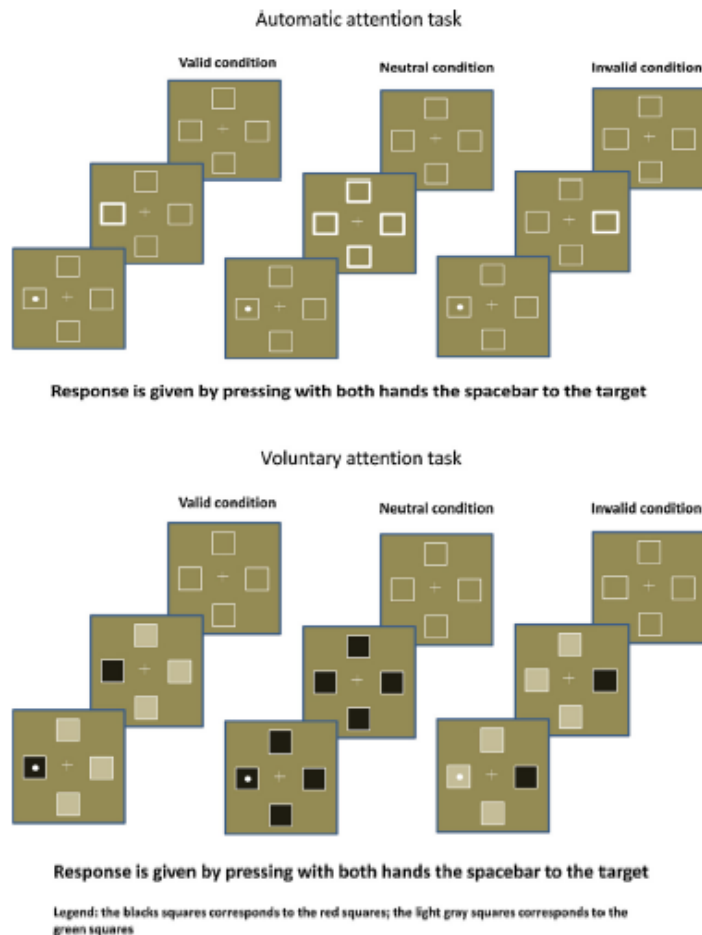


Fig. 1. Experimental representation of the different conditions of automatic and voluntary attention tasks.

three-way mixed-design ANOVA, with Group (DMD, age-matched and youngers 6–9) as a between-subjects factor, and Task (automatic, voluntary) and Condition (valid, neutral, neutral no-cue, and invalid cue) as within-subjects factors.

Error percentages were computed including omissions (no response to the target stimuli) and anticipations (response to the target stimuli before 150 ms).

Other dependent variables analyzed were: benefits (difference between RTs in the neutral condition and RTs in the valid condition), cost (difference between RTs in the invalid condition and RTs in the neutral condition) and attentional effect (difference between the RTs in the invalid and valid conditions) of attention.

All RT distributions were trimmed to exclude extreme scores beyond two standard deviations from the mean. Tukey's post hoc test or Fisher's LSD were used when required.

### 3. Results

The three-way ANOVA on weighted RTs reported the main effects of Group ( $F(2,47)=4.13$ ,  $p<.05$ ) and Condition ( $F(3,141)=3.89$ ,  $p<.01$ ). Mean weighted RTs were significantly slower (Tukey post hoc:  $p<.05$ ) for DMD (477 ms) and youngers 6–9 (480 ms), which did not differ from each other, than for the age-matched group (411 ms). This ratio between the RTs of the three groups is maintained in both the automatic and voluntary attention tasks (Fig. 2). Moreover, a significant Task  $\times$  Condition interaction was found ( $F(3,141)=10.57$ ,  $p<.001$ ; Fig. 3). Also, an intriguing trend was found concerning the Task  $\times$  Group interaction (Fig. 2). There was no significant difference between mean weighted RTs of the DMD group with those of the younger 6–9 group ( $p>.05$ ) which are significantly slower than those of the age-matched group ( $p<.01$ ) in the automatic attention task. The same ratio was found in the voluntary attention task.

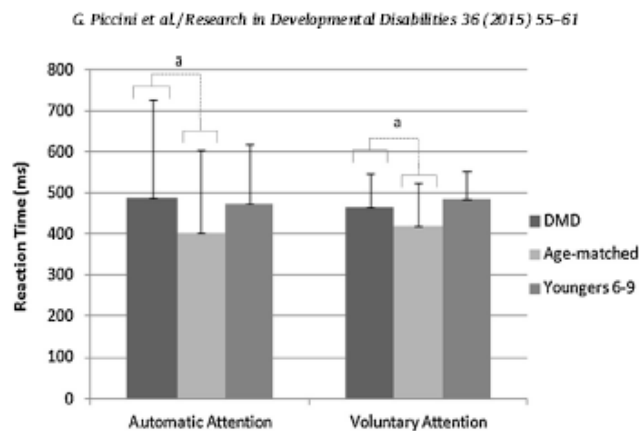


Fig. 2. Mean weighted RT for DMD, Age-matched and Youngers 6–9 in the automatic and voluntary attention tasks. \* $p < .05$ .

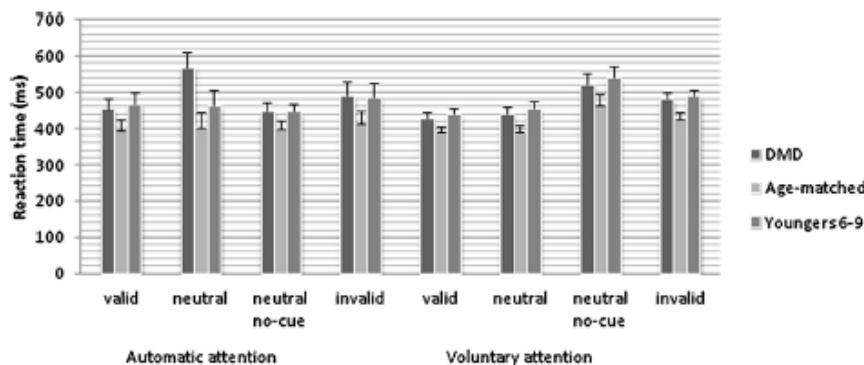


Fig. 3. Mean weighted RT for DMD, Age-matched and Youngers 6–9 in all conditions of automatic and voluntary attention tasks.

### 3.1. Voluntary visuospatial attention

The two-way ANOVA on weighted RTs in the voluntary task showed the main effects of Group ( $F(2,50) = 4.66, p < .01$ ), Condition ( $F(3,150) = 19.29, p < .01$ ) but Group  $\times$  Condition interaction was not statistically significant. Post hoc analysis confirmed that mean weighted RTs of DMDs and youngers 6–9 did not differ from each other, but were both significantly slower than those of the age-matched group (Fisher's LSD<sup>1</sup>  $p < .05$  and  $p < .01$  respectively).

### 3.2. Automatic visuospatial attention

The two-way ANOVA on weighted RTs in the automatic task reported only a trend for Group ( $F(2,50) = 2.73, p = .07$ ) and Condition ( $F(3,150) = 2.22, p = .08$ ). Post hoc analysis reported that mean weighted RTs of DMDs were significantly slower than those of the age-matched group ( $p < .05$ ), and did not differ from youngers 6–9. An unexpected post hoc effect in the automatic task was found for the DMD group, but not for the other groups: DMD children showed significantly slower weighted RTs for the neutral trials compared with the other three conditions (all values  $p < .05$ ). The weighted RTs for the neutral condition in DMD were even slower than those for the same condition in the other two groups (all  $p < .05$ ).

### 3.3. Cost, benefit and attentional effect

Mean values for costs, benefits and attentional effect are reported in Table 1. Even if no significant difference was observed between groups for costs, benefits and attentional effect in either the automatic or the voluntary attention tasks ( $p > .05$  in all cases), mean values showed larger costs, benefits and attentional effect for DMD and youngers 6–9 compared to

<sup>1</sup> Owing to Fisher's higher LSD sensitivity, this post hoc analysis was preferred in the two-way ANOVA.

Table 1

Mean value of costs, benefits and attentional effect for the three groups. All values are in ms.

	Costs (invalid-neutral)	Benefits (neutral-valid)	Attentional effect (invalid-valid)
Automatic attention			
DMD	–80	109	33
Age-matched	24	15	38
Youngers 6–9	28	–9	13
Voluntary attention			
DMD	42	8	54
Age-matched	16	17	33
Youngers 6–9	40	–6	41

Automatic and voluntary attention task.

the age-matched group in the voluntary task, and a larger attentional effect for DMD and youngers 6–9 than for the age-matched group in the automatic task. The lack of significance was probably due to the sample size of the experimental group (partial eta-squared and observed power for costs, benefits and attentional effect are respectively: .02, .12; .04, .23; .04, .24, revealing an effect size small to medium and a weak power analysis, not beyond the threshold of .8), even if the absence of the effects cannot be excluded.

#### 4. Discussion

Since both voluntary and automatic attention is driven by the neural circuits of the frontal cortex, and since dystrophin is normally produced in the deep pyramidal cells of the frontal lobes, the aim of this study was to examine the effects of dystrophin absence on attentional abilities.

By means of two orienting of attention tasks, adapted in order to minimize the motor component of response, we found that in the voluntary attention the DMD group's performance (both RTs and errors) was significantly worse than that of the age-matched group, and not statistically different from younger controls. In the automatic attention task as well, the performance of the DMD patients was less efficient compared with the age-matched controls and equal to that of the younger children, and there was a not significant larger attentional effect for DMD and youngers 6–9 than for age-matched participants. Surprisingly, and differently from the other two groups, DMD patients showed a worse performance in presence of neutral trials (all four squares blinking) than in the other trial conditions in automatic attention. We suggest that this effect could be due to higher difficulties of DMD patients to reduce the focus lens area (Castiello & Umiltà, 1990; Turatto et al., 2000) from one in which all the squares are visible to one in which only the square in which the target appears can be seen. An alternative explanation is that the effect could be due to a "crowding effect", i.e., the detrimental effect of the proximity of nearby items or contours on the visual perception of a stimulus (Lavie & de Fockert, 2003; Loomis, 1978), generated by the blinking of the four squares. In any case, this effect suggests a difficulty in automatic attention control.

The results of the present study confirm the previous report of a voluntary orienting of attention difficulties in DMD (De Moura et al., 2009). Furthermore, the results would suggest the presence of additional difficulties even of automatic orienting of attention in this pathology. This observation would indicate that the absence in DMD patients of full-length dystrophin expression, which mainly takes place in the frontal lobes, would negatively affect attentional control, in both its sub-components of voluntary and automatic visuospatial orienting. Therefore, we can presume that a normal expression of the protein dystrophin is crucial for a normal development of visuospatial attention skills. However, further studies supporting the difficulties also of automatic attention in patients with DMD are needful.

In addition, our data verify De Moura and colleagues' finding that 12-year-old DMD patients perform as well as 6–9 year-old children with typical development. These results reinforce the statement that the absence of full-length dystrophin expression is associated with a delayed maturation of visuospatial attention skills. We prefer to speak about "delay" instead of "deficit" because no normalized performance indices are available for the tasks we used, since they were ad hoc created for experimental needs. Furthermore, to the best of our knowledge, no standardized neuropsychological test assessing for automatic and voluntary orienting of attention does exist. The present study focused on attentional skills, but in the light of previous research (Wicksell et al., 2004) we cannot exclude that DMD patients are more generally affected in their executive control abilities.

#### 5. Conclusions

In conclusion, this study supports the previous report of voluntary attention deficit in DMD and extends the evidence to include also a deficit of the automatic attention system. Finally, we can reasonably state that DMD patients' development level of automatic and voluntary orienting of attention systems is below that expected for their age and corresponds to a delay of about three years. A delay of attention abilities may be responsible for many difficulties in daily life employments. Indeed, generalizing to clinical respects, the results of the present study fit into the framework of attentional difficulties of Duchenne patients, as indicated by the DMD-ADHD comorbidity described in Introduction. Therefore, the results of our study

suggest that a rehabilitative training should be addressed to strengthen not only the ability of voluntary orienting of attention, but also of the automatic one.

These conclusions are limited to DMD population of around 10 years old, with no intellectual disabilities and unimpaired functionality of the upper limbs. Moreover, a sample size of twenty may not be large enough to detect some of effects investigated and a larger DMD group is desirable in future studies. Finally, we did not control for kind of isoforms involved. The conclusions about automatic attention are therefore only indicative since there was not a clear significant effect. Future studies should clarify the issues of a possible automatic attention delay in DMD, what is exactly the role of dystrophin in the neurons subserving attention orienting and control and how this protein operates, and also investigate potential associations between site of mutation and behavioral phenotype.

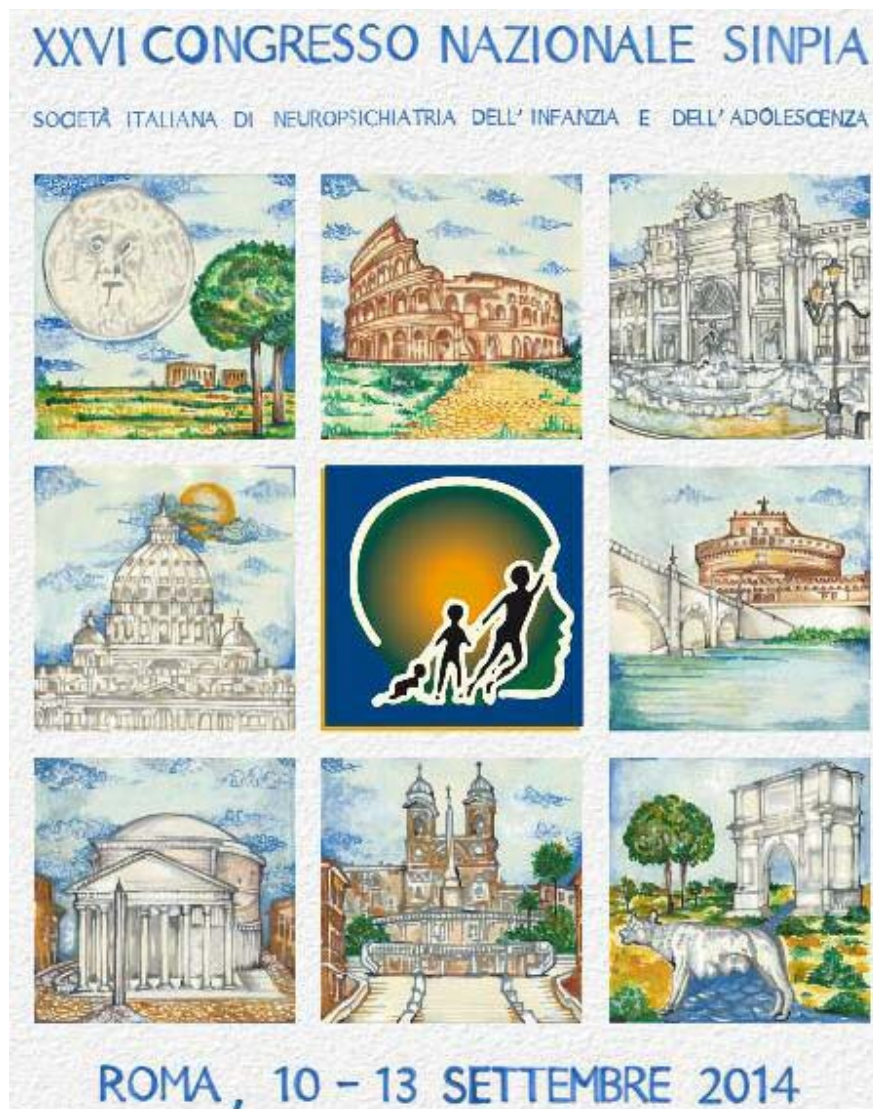
### Acknowledgements

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# ABSTRACT

relative all'ADHD

## **062 - DISTURBO DA DEFICIT D'ATTENZIONE E IPERATTIVITÀ (ADHD) E DISTURBI DELLO SPETTRO AUTISTICO (ASD): UN'ESPERIENZA DI TRATTAMENTO PSICOFARMACOLOGICO CON RISPERIDONE E ARIPIPAZOLO**

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I sintomi di iperattività, impulsività, e inattenzione (ADHD) sono spesso associati con disordini dello spettro autistico (ASD) e interferiscono con gli interventi comportamentali e con la qualità della vita (Gargano et al 2011). Numerosi studi evidenziano l'efficacia di risperidone e di aripiprazolo nel trattamento dei disturbi comportamentali associati ad ASD.

La nostra ricerca valuta efficacia e tollerabilità di risperidone e aripiprazolo in bambini e adolescenti con comorbidità ASD – ADHD.

11 soggetti in trattamento con Aripiprazolo e 12 con Risperidone sono stati sottoposti a valutazione psicocomportamentale (CGI, ADHD-Rating Scale-IV, C-GAS, sub scale H e D della CPRS) prima dell'inizio del trattamento farmacologico (T0), dopo 12 (T1) e dopo 24 settimane dall'inizio della terapia. La presenza di effetti collaterali è stata valutata con una checklist (side effect review-RUPP, 2005).

Il confronto evidenzia differenze significative a favore di Aripiprazolo dopo 12 settimane di trattamento alle scale CGI-I, C-GAS, ADHD-rs e CPRS H. A T 2 non si evidenziano differenze statisticamente significative tra i due gruppi.

I nostri risultati confermano l'efficacia dei neurolettici atipici nel trattamento di soggetti con comorbidità complesse come ASD e ADHD, sebbene i due farmaci mostrino profili di efficacia e tollerabilità differenti.

## **102 - ATTENTION DEFICIT HYPERACTIVITY DISORDER DRUGS USE CHRONIC EFFECTS (ADDUCE): PROGETTO EUROPEO DI FARMACOVIGILANZA SUL METILFENIDATO IN PAZIENTI CON ADHD**

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Il farmaco d'elezione per il trattamento dell'ADHD è il Metilfenidato. Nell'ambito del 7PQ il progetto ADDUCE è stato disegnato con lo scopo di valutare gli eventi avversi a lungo termine del Metilfenidato (MPH).

Lo studio prospettico recluterà 800 bambini e adolescenti con ADHD che intraprendono per la prima volta il trattamento con MPH, 400 ADHD che non assumono MPH e 400 controlli. Partecipano al progetto Italia, Germania, Ungheria, Gran Bretagna. Il protocollo prevede 4 visite semestrali con un attento monitoraggio neurologico, psichiatrico, cardiovascolare e dei parametri di crescita.

Attualmente risultano arruolati 629 ADHD con MPH, 348 ADHD che non assumono MPH e 193 soggetti di controllo.

In Italia contribuiscono al progetto: Università Cagliari (121 soggetti), UONPIA Lodi (39), UONPIA Brescia (34), Università Messina (79), Policlinico Milano (10), IRCCS Stella Maris (32) e recentemente San Donà di Piave. Il drop-out risulta circa il 25%.

Il progetto ADDUCE, consentirà di rispondere a specifiche domande riguardo la prevalenza, significatività clinica, i fattori moderatori e mediante le quattro specifiche classi di eventi avversi a lungo termine dell'uso cronico di MPH. Lo studio mostra come sia possibile svolgere studi indipendenti tra numerosi centri (7 italiani) di diversi paesi europei.



## 105 - **RICONOSCIMENTO DELLE EMOZIONI FACCIALI IN BAMBINI CON ADHD O DISTURBO DELLO SPETTRO AUTISTICO (ASD): EFFETTI DEL METILFENIDATO**

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Confrontare ADHD, ASD e soggetti di controllo, attraverso task di processamento delle emozioni facciali della batteria Amsterdam Neuropsychological Test (ANT) e valutare l'effetto del Metilfenidato.

Sono stati valutati i Tempi di Reazione alle risposte corrette (RTc), i Tempi di Reazione alle risposte errate (RTe) e il numero di errori (Errori) per i task Facial Recognition (FR), Identification Facial Emotion (IFE) e Matching Facial Emotion (MFE), in 48 ADHD, 32 ASD e 36 controlli di età 6-14 e  $QI > 70$ . Gli stessi task sono stati risomministrati ad un sottogruppo di ADHD con MPH.

Gli ADHD drug-free e gli ASD sono risultati più lenti e meno accurati rispetto ai controlli in FR e IFE e nel matching di alcune emozioni. Nel processamento della "sorpresa" sia ADHD che ASD hanno mostrato RTc più lunghi rispetto ai controlli (ASD  $p < .001$ , ADHD  $p = .018$ ).

Il MPH ha determinato un significativo miglioramento nel riconoscimento delle facce sia per velocità (RTc:  $p = .023$ ) che accuratezza ( $p < .001$ ). Un aumento dell'accuratezza è stato riscontrato anche in IFE ( $p = .004$ ) e MFE ( $p < .001$ ) specialmente per la "felicità".

Deficit specifici nel processamento delle emozioni sono presenti sia negli ADHD che negli ASD. Il metilfenidato contribuisce a ridurre tale compromissione negli ADHD.

## 106 - **Comorbidità associate all'ADHD**

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Molteplici sono le comorbidità psichiatriche e mediche presenti in bambini e adolescenti con ADHD spesso associate all'età e allo sviluppo. Il profilo nella popolazione italiana è ancora incerto.

Sono stati analizzati i dati clinico-anamnestici presenti nel database del Registro Lombardo di nuovi pazienti valutati dai 18 Centri di Riferimento ADHD nel periodo Giugno 2011-Maggio 2014.

La diagnosi di ADHD e di eventuali comorbidità psichiatriche è stata effettuata secondo i criteri del DSM-IV-TR e mediante valutazione clinico-testale (scale Weschler, CBCL, Conners', K-SADS-PL).

980 di 1.739 casi sospetti (66%) hanno ricevuto una diagnosi di ADHD (M:F=6:1; età mediana:9aa; range:5-17aa), nel 21% dei casi era presente familiarità per ADHD. 642 (65%) pazienti presentavano almeno un altro disturbo psicopatologico (disturbi dell'apprendimento:35%, disturbo oppositivo/provocatorio:14%, disturbi del sonno:13%, disturbi d'ansia:8%); mentre 77 (8%) avevano in associazione altra condizione medica cronica (45 di tipo neurologico, 34 respiratorio). L'età alla diagnosi più elevata e la diagnosi di ADHD erano associati con un maggior rischio di presentare disturbi psichiatrici associati (OR per età:1,45; OR per ADHD: 1,29); mentre, nel gruppo ADHD rispetto ai non ADHD, avevano un rischio maggiore i soggetti che frequentavano la scuola secondaria ( $p = 0,0006$ ), quelli supportati da insegnante di sostegno ( $p < 0,0001$ ), bambini con ritardo nell'acquisizione del linguaggio ( $p = 0,0004$ ) e i nati all'estero ( $p = 0,0339$ ).

Nei pazienti con ADHD è importante valutare e monitorare sistematicamente l'intero spettro delle possibili comorbidità psicopatologiche associate, anche tenendo conto della loro evoluzione, comparsa e associazione con particolari tappe cronologiche e psicologiche dello sviluppo.

### **113 - EFFETTI DEL METILFENIDATO NEL LUNGO TERMINE SULLA CRESCITA IN BAMBINI E ADOLESCENTI CON ADHD. REVISIONE SISTEMATICA DELLA LETTERATURA NELL'AMBITO DEL PROGETTO EUROPEO ADDUCE**

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Effettuare una revisione sistematica degli studi che indagano gli effetti nel lungo termine del metilfenidato sulla crescita e la maturazione puberale in soggetti ADHD.

Sono state utilizzate le banche dati *Embase* (1980-Giugno 2011), *PsycINFO* (1999-Giugno 2011) e *Medline* (1957-Agosto 2013). La ricerca è stata limitata agli studi in bambini e adolescenti, gli studi su adulti sono stati esclusi.

Sono stati inclusi 16 studi per un totale di 3140 soggetti (range= 34-485; media= 177.86; DS= 130.15; mediana = 140), il 66.7% di sesso maschile (2096/1044). Le analisi sulla crescita sono state effettuate in circa 2035 soggetti.

Sei degli studi inclusi non supportano l'ipotesi di una possibile correlazione tra l'uso degli stimolanti e un deficit di crescita. 10 studi (n = 1781) mettono invece in evidenza effetti significativi sugli z score di altezza, peso e BMI. Il deficit di altezza risulta maggiormente evidente durante i primi 6-12 mesi di terapia con una successiva normalizzazione.

Il trattamento con MPH nel lungo termine può determinare un lieve deficit di crescita, anche se i meccanismi biologici sottostanti non sono ancora stati chiariti. Il progetto ADDUCE, con un rigoroso follow up consentirà di rispondere e chiarire alcuni quesiti ancora irrisolti.

### **116 - INTERAZIONE TRA FATTORI NEUROPSICOLOGICI E NEUROLINGUISTICI IN BAMBINI CON DEFICIT DI ATTENZIONE E IPERATTIVITÀ, DISTURBI SPECIFICI DI LINGUAGGIO CON O SENZA COMORBIDITÀ: POPOLAZIONI CLINICHE A CONFRONTO**

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La comorbidità tra ADHD e Disturbi del Linguaggio (DSL) raggiunge quasi il 50%. Entrambe le patologie presentano una compromissione di alcune funzioni cognitive ma, al momento, sono ancora scarse le ricerche che hanno effettuato studi comparativi. Ci siamo posti l'obiettivo di identificare le componenti neuropsicologiche che meglio differenziano tre gruppi di bambini prescolari con ADHD, DSL e ADHD in comorbidità con DSL.

Sono stati reclutati 42 bambini con ADHD, 30 ADHD+DSL, 32 DSL e 25 controlli. Le funzioni esecutive indagate sono: controllo inibitorio, attenzione, memoria di lavoro, pianificazione e fluency verbale. Le abilità linguistiche prese in esame riguardano gli aspetti lessicali, sintattici e narrativi.

L'analisi delle componenti principali ha identificato 4 fattori che spiegano il 62% della varianza totale: processamento rapido verbale, attenzione, controllo inibitorio / pianificazione, abilità linguistiche. Due funzioni discriminanti differenziano in maniera significativa i 3 gruppi (p < .001): la prima funzione discrimina ADHD+DSL dal gruppo DSL e ADHD; la seconda funzione discrimina il gruppo ADHD dai DSL e ADHD+DSL.

Una specifica interazione tra componenti cognitive e linguistiche è in grado di discriminare i 3 gruppi studiati e identificare differenti organizzazioni funzionali nell' ADHD e nei DSL con o senza comorbidità.

## **117 - OVERLAPPING TRA I DISTURBI DELLO SPETTRO AUTISTICO (DSA) E IL DISTURBO DA DEFICIT DELL'ATTENZIONE E IPERATTIVITÀ/IMPULSIVITÀ (ADHD)**

**F. Craig**

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La recente pubblicazione della quinta edizione del Manuale Diagnostico e Statistico dei Disturbi Mentali (DSM-5) introduce rilevanti novità individuando i Disturbi del Neurosviluppo e la diagnosi in comorbidità dei DSA e ADHD.

Lo scopo dello studio è di valutare le caratteristiche cliniche comuni o distintive dei DSA, ADHD e del fenotipo combinato (DSA+ADHD).

Il campione è costituito da 181 pazienti: 43 bambini con diagnosi di DSA isolato, 51 bambini con diagnosi di ADHD isolato, 31 bambini con DSA+ADHD in comorbidità e 56 bambini controllo. In tutti i soggetti partecipanti allo studio sono stati somministrati test standardizzati (CBCL, CSR, SNAP-IV, SCQ e VABS).

I gruppi ADHD e DSA+ADHD riportano una maggiore presenza di sintomi d'inattenzione/iperattività rispetto ai gruppi DSA e controllo. Il gruppo DSA+ADHD mostra una severità maggiore di sintomi autistici rispetto ai gruppi DSA, ADHD e Controllo. Nei gruppi DSA+ADHD e DSA è stata riscontrata una maggiore compromissione del funzionamento adattivo. Infine, i disturbi esternalizzanti sono maggiormente presenti nei gruppi DSA+ADHD e ADHD, mentre i disturbi internalizzanti sono equamente rappresentati nei gruppi clinici.

I dati emersi da questo studio suggeriscono che il gruppo DSA+ADHD individua un fenotipo combinato con caratteristiche cliniche e severità differenti rispetto alle forme isolate di ADHD e DSA.

## **120 - REBOXETINA E ADHD: CASISTICA CLINICA E REVISIONE DELLA LETTERATURA**

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La Reboxetina è un farmaco inibitore selettivo del reuptake della Noradrenalina che può essere utilizzato nel trattamento dell'ADHD nei casi considerati non responders alla terapia con Metilfenidato (circa 30% dei casi), o quando la stessa terapia non è ben tollerata dal paziente.

Studio clinico in aperto in un gruppo di bambini e adolescenti, afferiti presso il Centro Regionale per l'ADHD dell'ULSS 16 di Padova, sottoposti per 8 settimane a terapia con Reboxetina (4 mg/die). Per ogni paziente è stata effettuata una valutazione clinica, comprendente test strutturati somministrati al paziente, ai genitori e agli insegnanti (SNAP-IV, CGI ADHD-S, SCARED, CBCL/YSR, CDRS-R:S/CPRS-R:S/CTRS-R:S, SDQ-A/P/T, TRF e CDI) e test neuropsicologici (CPT-II, TOL), ad intervalli prefissati (pre-, inter- e post-trattamento). Analisi intermedie hanno permesso di monitorare l'efficacia e la tollerabilità della terapia in corso.

Partendo da confronto dei dati emersi in letteratura, verranno presentati i risultati emersi dalla revisione di una casistica di 28 pazienti di sesso maschile, di età media di 10 aa e 6 mesi (range: 5.6 aa - 14.5 aa).

## **124 - TRATTI AUTISTICI E DISREGOLAZIONE EMOZIONALE IN BAMBINI CON ADHD**

**G. de Rénoche, M. Ronchese, D. Polezzi, D.G. Taratufolo, E. Poletto, L. Bianchin**

*Unità Operativa Complessa di Neuropsichiatria Infantile e dell'Adolescenza, ULSS 16 Padova*

Recenti lavori (Biederman, 2012,2010, Kotte 2013) hanno rilevato la presenza di sintomi dello spettro autistico e di alterata regolazione emozionale in bambini con e senza ADHD mediante l'utilizzo delle scale empiriche della Child Behavior Checklist (CBCL).

Analisi retrospettiva condotta su un gruppo di bambini e adolescenti, afferiti presso il Centro Regionale per l'ADHD dell'ULSS 16 di Padova.

Con riferimento alla letteratura citata, sono state prese in considerazione le sottoscale di derivazione empirica della CBCL compilata dai genitori, ottenendo due ulteriori sottoscale: la prima indicata come CBCL-AT (CBCL-Tratti Autistici), derivante dalla somma dei punteggi T delle tre sottoscale Withdrawn, Social Problems e Thought Problems; la seconda, ricavata dalla somma dei punteggi T delle sottoscale Anxiety/Depression, Aggression e Attention, con l'obiettivo di individuare i soggetti che presentavano anche significative difficoltà a livello di auto-regolazione emozionale.

Verranno presentati i risultati emersi dall'analisi di una casistica relativa a più di 200 soggetti affetti da ADHD mediante CBCL relativamente ai sintomi di disregolazione emozionale e di tipo autistico.

## **133 - EFFICACIA E TOLLERABILITÀ DEL METILFENIDATO A RILASCIO MODIFICATO NELL'ADHD: ESPERIENZA PRESSO L'ISTITUTO GASLINI DI GENOVA**

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Il Disturbo da Deficit di Attenzione e Iperattività (ADHD) è una patologia frequente dell'età evolutiva che può portare a significativa compromissione della qualità della vita. La farmacoterapia si avvale di Metilfenidato a rilascio immediato o Atomoxetina. La sorveglianza farmacologica si attua con iscrizione del paziente nel registro nazionale ADHD. Recentemente in Italia è disponibile il Metilfenidato a rilascio modificato, che consente un rilascio immediato di Metilfenidato, seguito dal rilascio lento della restante quota di farmaco, permettendo la monosomministrazione giornaliera. L'obiettivo dello studio è di valutare l'efficacia e la tollerabilità del Metilfenidato a rilascio modificato in pazienti con ADHD.

In 9 pazienti, 8 maschi e 1 femmina, di età media di 9 anni, con diagnosi di ADHD è stata avviata la terapia con Metilfenidato a rilascio modificato, dopo prima somministrazione di Metilfenidato a rilascio immediato in regime protetto, e follow-up clinico e psicodiagnostico a 6 mesi.

In 8 pazienti il follow-up ha mostrato buona efficacia e tollerabilità del farmaco. Soltanto in un paziente è stata sospesa la terapia per mancata efficacia, senza comparsa di effetti collaterali.

La nostra esperienza conferma che il Metilfenidato a rilascio modificato è un farmaco efficace e ben tollerato nei pazienti con ADHD.

### **136 - IL PASSAGGIO ALLA TERAPIA CON METILFENIDATO A RILASCIO MODIFICATO NEI SOGGETTI AFFETTI DA ADHD IN CARICO AL CENTRO DI RIFERIMENTO DI BORGOMANERO**

**F. Guccione**

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Nell'ottobre 2013 è entrato in commercio in Italia il metilfenidato a Rilascio Modificato. Pertanto, ai pazienti che erano in terapia con la formulazione a Rilascio Immediato, è stato proposto il passaggio alla formulazione a R.M., dopo una corretta illustrazione dei vantaggi e delle criticità.

N.18. pazienti di età tra 8 e 15 anni in carico presso il Centro di Borgomanero, nell'ultimo trimestre 2013, sono passati alla formulazione a R. M.

Dei 18 pazienti passati alla formulazione a R.M.: 17 hanno accettato senza difficoltà e con beneficio la nuova formulazione; hanno ridotto il numero di somministrazioni della terapia, senza essere costretti ad assunzioni in orario scolastico.

In un unico caso i genitori, hanno richiesto di ritornare alla terapia a R.I., accusando scarso beneficio terapeutico durante la mattinata.

Il passaggio alla terapia a R.M. ha confermato i vantaggi di questa formulazione: riduzione del numero di somministrazioni e maggiore durata d'azione della terapia nell'arco della giornata.

### **138 - FATTORI DI RISCHIO DI SINTOMI ADHD IN BAMBINI AFFETTI DA DISTURBI DELLO SPETTRO AUTISTICO**

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Nel corso degli anni diversi autori hanno riportato sintomi ADHD in pazienti con Disturbi dello Spettro Autistico (DSA), tuttavia in letteratura mancano studi sui fattori di rischio di sintomi ADHD nei DSA.

L'obiettivo di questo studio è individuare sintomi ADHD in un campione DSA confrontandoli con un campione di controllo ed identificare, nel campione DSA, fattori di rischio per lo sviluppo di sintomi ADHD (in particolare fattori di rischio del bambino, familiari e legati alla gravidanza).

Sono stati arruolati 67 bambini affetti da DSA e 53 controlli affetti da malattie chirurgiche pediatriche.

Il 55% dei pazienti con DSA ha riportato sintomi ADHD alle CPRS (Conners' Parent Rating Scale), il 61% alla SNAP-IV (Swanson, Nolan and Pelham Questionnaire) inattenzione e il 49% alla SNAP-IV iperattività/impulsività, con una differenza significativa rispetto al controllo. L'ANOVA ha mostrato che l'età del bambino, il ritardo del linguaggio, l'enuresi, le allergie, le comorbidità con il Disturbo Oppositivo Provocatorio e con le Disabilità intellettive sono associate ad un incremento di sintomi ADHD nei bambini DSA.

I risultati di questo studio sono un'ulteriore evidenza di una condivisione di meccanismi patogenetici comuni sottostanti i DSA e l'ADHD e suggeriscono la necessità di promuovere ulteriori studi in quest'ambito.

### **139 - VALUTAZIONE DEGLI EFFETTI CARDIOVASCOLARI ACUTI DEL METILFENIDATO A RILASCIO IMMEDIATO IN BAMBINI ED ADOLESCENTI CON ADHD**

**M. Lamberti<sup>1,3</sup>, E. Germanò<sup>1</sup>, D. Italiano<sup>3</sup>, R. Siracusano<sup>1</sup>, L. Guerriero<sup>1</sup>, G. D'Amico<sup>2</sup>, A. Alquino<sup>1</sup>, M.P. Calabrò<sup>2</sup>, E. Spina<sup>3</sup>, A. Gagliano<sup>1</sup>**

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Il gold standard per il trattamento del Disturbo da Deficit di Attenzione con Iperattività (ADHD) è il metilfenidato (MPH). Scopo della nostra ricerca è studiare il rischio cardio-tossico del MPH, durante il picco plasmatico del MPH a immediato rilascio (MPH-IR).

Sono stati arruolati 54 pazienti drug-naive con diagnosi di ADHD. Tutti i pazienti sono stati sottoposti ad esame ECG, in basale (To) e a distanza di 2 ore dall'assunzione del farmaco (T1), dopo che per essi era stata stabilita la dose terapeutica di MPH. Sono stati quindi valutati e confrontati la media corretta del QT (QTc), il tempo di dispersione del QT (QTd) e l'intervallo dell'onda T (TpTe).

Non si sono evidenziate modifiche clinicamente significative di nessuno dei parametri analizzati dopo l'assunzione della dose di metilfenidato. La FC ed i valori del TpTe sono variati in modo statisticamente significativo da To a T1, ma entrambi i valori si sono sempre mantenuti all'interno dell'intervallo di normalità e non sono variati in modo clinicamente significativo.

I risultati della nostra ricerca mostrano che durante le prime ore dall'assunzione del MPH non si rilevano modifiche elettrocardiografiche che configurano un rischio clinico. I nostri dati confermano, con dati obiettivi, la relativa sicurezza cardiovascolare del MPH.

### **141 - CENTRO DI RIFERIMENTO ADHD: UN MODELLO ORGANIZZATIVO IN SERVIZIO TERRITORIALE**

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A partire dalla Legge istitutiva dei Centri di riferimento ADHD e dalle linee guida nazionali e internazionali sul trattamento del disturbo che vedono la migliore efficacia in trattamenti combinati (psicoterapia cognitivo comportamentale e farmaco), nei servizi sanitari territoriali per età evolutiva si è verificata un'estrema difficoltà nell'attuazione degli interventi psicoterapeutici e psicoeducativi per la carenza di risorse disponibili.

Nel poster verrà descritto il modello organizzativo di un Centro di Riferimento per ADHD realizzato in integrazione tra UUOCC NPI e PSI attraverso l'individuazione di quote orarie per operatori nel rispetto degli assetti organizzativi preesistenti.

Il Centro si configura a dimensione provinciale, sovrazonale rispetto alle Unità Territoriali Distrettuali dei Servizi per Età Evolutiva, in una realtà regionale con presenza di poli universitari, e fornisce prestazioni anche ad utenti esterni provenienti da ASL limitrofe.

Nel poster verranno fornite informazioni:

sulle caratteristiche dei percorsi terapeutici proposti per bambini e genitori e su i loro esiti

sulle modalità di integrazione utilizzate per inserire le attività effettuate nel Centro con la presa in carico globale realizzata nella dimensione distrettuale

sulle modalità di reperimento di risorse aggiuntive tramite la cogestione con Cooperative Accreditate.

Verranno altresì fornite considerazioni finali su punti di forza e criticità del modello.



## **146 - CARATTERIZZAZIONE DEL DISTURBO DI AUTO-REGOLAZIONE DELLE EMOZIONI (DESR) IN BAMBINI PRESCOLARI CON ADHD MEDIANTE L'USO DELLA CBCL: UNO STUDIO CASO-CONTROLLO**

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Il Disturbo di Auto-Regolazione delle Emozioni (Deficient Emotional Self-Regulation: DESR) è caratterizzato da uno specifico deficit a carico dei meccanismi omeostatici che controllano il livello di "arousal" fisiologico in presenza di forti emozioni. Lo scopo della ricerca è verificare se le dimensioni della Child Behavior Checklist per genitori (CBCL) e insegnanti (TRF) permettono di identificare la DESR in bambini prescolari con ADHD.

Sono stati reclutati 80 bambini prescolari con ADHD (età media in mesi:  $58,4 \pm 9$ ) e 99 controlli ( $60,0 \pm 8$ ).

CBCL e TRF 1½-5, Scala Leiter-R, intervista strutturata ai genitori per il profilo psicopatologico (PAPA).

Utilizzando i punteggi CBCL e TRF delle dimensioni: Ansia / Depressione (A/D), Problemi Attentivi (AP) e Comportamenti Aggressivi (AB), l'analisi delle curve ROC mostra soglie lievemente più basse nei prescolari rispetto ai bambini più grandi ( $A/D \geq 59$ ,  $AP \geq 60$ ,  $AB \geq 59$ ). Prescolari con DESR presentano inoltre alta comorbidità con ansia ( $P < 0,01$ ), disturbo oppositivo-provocatorio ( $P < 0,01$ ) e maggiore compromissione sociale ( $P < 0,05$ ) rispetto al gruppo ADHD senza DESR.

Le differenze rilevate richiedono un piccolo ma significativo aggiustamento dei valori di soglia usati per definire la presenza della DESR nella prima infanzia mediante CBCL e TRF.

## **151 - ADHD, DISTURBO OPPOSITIVO PROVOCATORIO, DISTURBO DELL'UMORE: QUANDO LA DIAGNOSI MULTIPLA IN ETÀ EVOLUTIVA "NASCONDE" IL DISTURBO TRAUMATICO DELLO SVILUPPO**

**C. Olivito**

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In età evolutiva è necessario, a volte, sia che si ricorra alla diagnosi categoriale (DSM) che a quella dimensionale, l'utilizzo di più categorie/dimensioni per poter descrivere in maniera esaustiva il pattern comportamentale e il funzionamento interno del paziente, non arrivando però a individuarne il "nucleo" psicopatologico. Anche se non inserito nella quinta versione del DSM come proposto dal Child Traumatic Stress Network (CTSN), il tenere presente i criteri diagnostici per il Disturbo traumatico dello sviluppo (van der Kolk, 2005), consente al neuropsichiatra infantile di inquadrare correttamente i pazienti "complessi" o "difficili".

L'obiettivo di questo lavoro è quello di sottolineare come i sintomi, soprattutto quelli "esternalizzanti", riscontrabili in età evolutiva, possano essere inquadrati non soltanto in una o più categorie del DSM, ma anche nel Disturbo traumatico dello sviluppo.

Confronto tra i criteri diagnostici di alcuni dei disturbi dell'età evolutiva riportati nel DSM-IV e i criteri diagnostici del Disturbo traumatico dello sviluppo.

La diagnosi multipla in età evolutiva può nascondere il Disturbo traumatico dello sviluppo.

## **156 - IL RUOLO DEI RETROVIRUS ENDOGENI UMANI (HERVS) NEL DISTURBO DA DEFICIT DI ATTENZIONE CON IPERATTIVITÀ (ADHD)**

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Numerose evidenze scientifiche suggeriscono che gli HERVs sono implicati nello sviluppo di molteplici malattie complesse con eziologia multifattoriale e forte ereditabilità, tra cui alcuni disturbi del neurosviluppo quali la schizofrenia e l'autismo infantile. L'ADHD è un disturbo del neurosviluppo, derivante da una complessa interazione di fattori genetici, biologici ed ambientali. Scopo dello studio è stato analizzare i livelli di espressione di 3 famiglie HERVs (HERV-H, K e W) nei pazienti con ADHD.

L'espressione dell'mRNA retrovirale è stata valutata nelle cellule polimorfonucleate del sangue periferico di 30 soggetti con ADHD e 30 controlli tramite un'analisi quantitativa condotta tramite RT-PCR.

I livelli di espressione della famiglia HERV-H sono risultati significativamente più alti nei pazienti con ADHD rispetto ai controlli. Al contrario, non sono state evidenziate differenze statisticamente significative nei livelli di espressione delle altre 2 famiglie considerate.

I risultati esposti indicano che, per le loro caratteristiche funzionali, gli HERVs possono rappresentare un anello di congiunzione tra fattori genetici, biologici ed ambientali ed il fenotipo clinico del disturbo. La verifica dei risultati riportati in una popolazione più ampia di pazienti con ADHD, renderà possibile approfondire il ruolo della famiglia HERV-H nella fisiopatologia dell'ADHD. Allo stesso tempo permetterà di chiarire ulteriormente il ruolo degli HERVs nei disturbi del neurosviluppo.

## **177 - CARATTERISTICHE DEL SONNO IN BAMBINI ADHD IN ETÀ PRESCOLARE: MISURE ATTIGRAFICHE E REPORT DEI GENITORI**

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Nonostante i problemi di sonno siano frequenti nei bambini ADHD, in epoca precoce, non è stato condotto nessuno studio oggettivo nei bambini prescolari affetti da ADHD. Abbiamo pertanto valutato il pattern del sonno in prescolari ADHD utilizzando misurazioni oggettive (attigrafia) e questionari del sonno somministrati ai genitori.

25 bambini ADHD (24 M; 5 F); età media  $5.39 \pm 1.03$  anni (range: 48-69 mesi) e 17 bambini sani (12 M; 10 F); età media  $5.33 \pm 1.11$  anni (range: 48-71 mesi). Misure: registrazioni attigrafiche per 5-7 notti consecutive e somministrazione di questionari e diari del sonno ai genitori.

La durata media del sonno e i parametri del sonno non sono differenti nei due gruppi. I "cattivi dormitori" sono presenti in 10/25 (40%) ADHD e in 2/17 (11,8%) controlli. Gli ADHD "cattivi dormitori" mostrano un aumento di movimenti nei parametri attigrafici (mean activity e activity index) vs. i "buoni dormitori" e una media degli episodi di veglia più alta. L'analisi dei questionari del sonno evidenzia la difficoltà di addormentamento come problema prevalente.

Lo studio conferma un incremento dell'attività motoria e problemi di addormentamento in prescolari ADHD. L'identificazione precoce dei disturbi del sonno può avere importanti implicazioni per la scelta del trattamento.

## **179 - DISTURBO DEGLI APPRENDIMENTI NON VERBALI: COMORBIDITÀ ASSOCIATA ALL'ADHD O NUOVA ENTITÀ NOSOLOGICA?**

**L. Zoccante, F. Boscaini, A. Beggiato, K. Battistella, G. Scrinzi, B. Berlese**  
*U.O.C. Neuropsichiatria Infantile A.O.U.I. Verona*

L'ADHD e il Disturbo degli Apprendimenti NonVerbali ( NonVerbal Learning Disorder, NLD) sono due disturbi distinti? Dalla nostra valutazione, il NLD è spesso diagnosticato come ADHD associato a Disturbo dell'Apprendimento. Il profilo neuropsicologico non sempre è sufficiente a differenziare ADHD e NLD, specialmente tra i 7 e i 12 anni. L'esame neurologico è fondamentale per distinguere i due disturbi.

64 nuovi pazienti (7-12 anni; esaminati da Gennaio 2013 a Maggio 2014) sottoposti a valutazione cognitiva e neuropsicologica e valutazione neurologica. Sono stati inoltre approfonditi gli aspetti psicopatologici mediante interviste a genitori ed insegnanti.

18 pazienti con ADHD sono risultati avere un quadro riconducibile a NLD. Questi pazienti differivano da quelli con ADHD perché presentavano un disturbo neuroevolutivo più complesso caratterizzato da: disturbo della coordinazione, lassità legamentosa, manierismi e/o tic, disgrafia, disturbo della percezione.

I 18 pazienti sono giunti alla nostra osservazione per sospetto ADHD, hanno invece ricevuto una diagnosi di NLD. La diagnosi differenziale è importante perché i quadri necessitano di differenti prese in carico. Inoltre il NLD, soprattutto nelle sue forme più severe, potrebbe spiegare i quadri di Disturbo dello Spettro Autistico Atipici.

## **213 - ADHD VS SLUGGISH COGNITIVE TEMPO: DUE ENTITÀ CLINICHE DIVERSE O VARIANTI DELLO STESSO DISTURBO? CASISTICA PERSONALE**

**E. Biondi ed Equipe multidisciplinare**

*Associazione J.F.Kennedy, Centro di riabilitazione neuro psicomotoria, Acireale, Catania*

Il termine Sluggish Cognitive Tempo (SCT) definisce un particolare tipo di disturbo dell'attenzione caratterizzato da bassa attivazione e lentezza cognitiva. Attualmente la SCT viene inglobata all'interno del deficit d'attenzione non associato a iperattività/impulsività (ADD), tuttavia numerosi e recenti studi dimostrano un grado di ipoattivazione, in contrapposizione alla iperattivazione caratteristica dell'ADHD. Il recente DSM V elimina la classificazione in diversi sottotipi, prestando importanza ai sintomi con cui si manifesta un disturbo, non facendo mai riferimento al disturbo SCT, a conferma della diversa entità clinica rispetto all'ADHD. I sintomi predittivi di SCT sono rappresentati da lentezza motoria e mentale, sognare ad occhi aperti, apatia, facilità alla noia e alla confusione. Altra caratteristica è la frequente associazione con sintomi internalizzanti quali ansia, depressione, disregolazione emotivo-affettiva, spesso difficoltà relazionali e scolastiche. L'obiettivo di questo studio è quello di mettere a confronto, attraverso valutazioni neuropsicologiche (WISC IV, torre di Londra, CBCL, SNAP, Connersparents, test delle campanelle, prove MT) e risposta alla terapia riabilitativa, un gruppo di 6 bambini con diagnosi di ADHD di cui 2 con sintomi SCT, al fine di capire meglio le cause, i correlati e i meccanismi che stanno alla base dei disturbi. Conclusioni: Sebbene i sintomi SCT non siano classificabili all'interno di un quadro diagnostico preciso non significa che non possano essere utili per comprendere meglio il sottotipo ADD o aiutare a definire un nuovo disturbo dell'attenzione.

## **269 - CONDIVISIONE E MONITORAGGIO DEI PERCORSI DIAGNOSTICI E TERAPEUTICI IN NEUROPSICHIATRIA: IL PROGETTO ADHD LOMBARDIA**

**L. Reale<sup>1,2</sup>, M. Bonatti, E. Zanetti<sup>3</sup> a nome del Gruppo Regionale ADHD**

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<sup>2</sup> UONPIA, IRCCS "Ca' Granda", Ospedale Maggiore Policlinico e Università degli Studi di Milano, Milano

<sup>3</sup> UONPIA, Ospedale dei Bambini, A.O. Spedali Civili di Brescia, Brescia

Pochi studi dimostrano la sostenibilità della medicina basata sulle evidenze in Neuropsichiatria. L'obiettivo del Progetto è garantire a bambini e adolescenti che accedono ai 18 Centri di riferimento ADHD della Lombardia percorsi diagnostico-terapeutici appropriati e condivisi.

Il progetto, attivo dal 2011, prevede: la definizione dei percorsi diagnostico-terapeutici; l'istituzione di un Registro dei casi; iniziative di formazione e informazione.

La valutazione prevede 6 steps necessari (colloquio, esame neurologico, K-SADS, QI, CTRS, CPRS e CBCL, CGI-S). I Training (Child, Parent e Teacher) sono interventi di prima scelta associati al trattamento farmacologico per i casi gravi.

In tre anni sono stati identificati 1.739 nuovi pazienti di cui 980 (66%) con diagnosi confermata, di questi 642 (65%) presentavano almeno una comorbidità psichiatrica. L'84% ha ricevuto una prescrizione non farmacologica, il 3% solo farmacologica. La quasi totalità (96%) rimane in carico ai Centri per i trattamenti e i controlli previsti ad intervalli periodici (3, 6, 12, 18, 24 mesi). Attualmente 406 (65%) pazienti con ADHD sono monitorati in modo sistematico da oltre un anno dal momento della diagnosi.

Sono stati prodotti 3 libretti-guida informativi e una newsletter mensile (74 numeri; 4588 lavori scientifici segnalati). È stato, inoltre, organizzato un Convegno (scientifico, pubblico e indipendente) a cui hanno partecipato attivamente 451 interessati (32% psicologi, 24% insegnanti e genitori, 16% neuropsichiatri infantili).

Il Progetto ha consentito di sviluppare un monitoraggio continuo e sistematico delle cure che ha permesso di usare in modo appropriato le risorse sulla base dei bisogni, attivando progressivi e significativi miglioramenti per un'efficiente e omogenea qualità delle cure.

## **287 - SINDROME DA INATTENZIONE IPERATTIVITÀ/IMPULSIVITÀ (ADHD). ESPERIENZA DEL CENTRO DI RIFERIMENTO REGIONALE, SOD NEUROPSICHIATRIA INFANTILE- AOU OSPEDALI RIUNITI-PRESIDIO SALESI**

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L'ADHD è un disordine neuropsichico del bambino e dell'adolescente caratterizzato da inattenzione e impulsività/iperattività. Scopo dello studio è valutare le caratteristiche e l'efficacia dei farmaci della popolazione con ADHD afferita al Centro di Riferimento Regionale –Neuropsichiatria infantile dell'AOU di Ancona.

Per l'inquadramento diagnostico: Intervista K-SADS-PL; CPRS-R:S; CTRS-R:S;C-GAS;MASC;PARS; Test delle Campanelle; Torre di Londra; batteria MT per valutazione apprendimenti

Tra gennaio 2008 ed aprile 2014 sono stati valutati 135 bambini con ADHD (115 maschi; 20 femmine; età media: 9 anni 8 mesi.). L'87% presentava ADHD sottotipo combinato, il 71% una o più comorbidità ( DSA e DOP) e il 35% compromissione funzionale di grado moderato/severo. La terapia farmacologica (metilfenidato e atomoxetina) è stata intrapresa nel 18% dei casi ed interrotta in 2 bambini per l'insorgenza di effetti avversi.

Nei quadri moderati/severi che hanno intrapreso terapia farmacologica, l'associazione del farmaco con le terapie psicoeducative, comportamentali e neurocognitive è risultata efficace nel ridurre la gravità del quadro comportamentale.



## **293 - INTERVENTI NON-FARMACOLOGICI NELL'ADHD: APPLICAZIONE E RISULTATI**

**G. Vannini, F. Venditti, R. Leonetti**

*ASL10 Firenze*

Nel DSM-V è evidente la necessità di migliorare la nostra competenza di prevenzione, diagnosi e indirizzo terapeutico. Tenendo presenti i principi della Teoria Ecologica di Bronfenbrenner e della Teoria della Complessità si possono attuare interventi non-farmacologici che abbiano come obiettivo quello di migliorare la qualità di vita del nostro paziente.

Il presente studio vuole valutare l'efficacia dell'intervento psicoeducativo da solo o in combinazione con l'intervento farmacologico nei pazienti ADHD.

Sono stati valutati 114 pazienti ADHD con età compresa tra i 3 e i 18 anni. Gli interventi psicoeducativi considerati sono:

- a) interventi scolastici (laboratori per le prassie e le emozioni)
- b) counseling alla coppia genitoriale, valutazione della diade genitore-bambino o della triade genitori-figlio
- c) interventi nel piccolo gruppo.

Dall'analisi dei risultati emerge che l'intervento psicoeducativo serve a migliorare la qualità di vita del paziente riesce ad influenzare l'impulsività e l'iperattività, ma non il disturbo attentivo.

L'intervento farmacologico appare spesso indicato sebbene a causa dei problemi di compliance con i genitori si possa realizzare solo nel 5% dei casi.

## **294 - INTERVENTI PSICOEDUCATIVI NELL'ADHD**

**G. Vannini, F. Venditti**

*ASL10 Firenze*

Nel DSM-V è evidente la necessità di attuare interventi psicoeducativi che abbiano la funzione di migliorare la nostra competenza di prevenzione, diagnosi e indirizzo terapeutico.

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Dall'analisi dei risultati emerge che l'intervento psicoeducativo serve a contenere il disturbo ma non lo risolve mai completamente. Pertanto quando si sviluppa una buona compliance con la triade genitori-figlio è fondamentale il ricorso all'intervento farmacologico, mentre l'intervento psicoeducativo serve a migliorare la qualità di vita e quindi ha una valenza prevalente di tipo psico-sociale.

## 298 - STUDIO DELLA CONNETTIVITÀ EEG DEI FUSI DEL SONNO IN ALCUNI SOGGETTI CON ADHD

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\*\* Dipartimento di Ingegneria ed Architettura, Università degli studi di Trieste

Il sonno è considerato un utile ambito di studio rispetto alla correlazione tra funzioni cognitive e organizzazione della rete neurale. L'attività dei fusi viene correlata ad alcune funzioni cognitive e recentemente anche allo sviluppo emotivo.

Individuare possibili patterns di connettività EEG nel sonno di soggetti con ADHD.

Quattro soggetti con ADHD e 8 soggetti di controllo; fascia di età 7-11 anni. EEG con 21 elettrodi, riferimento biauricolare, frequenza di campionamento 512 Hz. Cinque epoche di un secondo, per ciascun soggetto, contenenti il fuso. Per estrarre le informazioni di connettività direzionale tra ogni coppia di canale è stato utilizzato il metodo spettrale multivariato della *Directed Transfer Function*. Per la misurazione della similitudine tra le matrici DTF è stata valutata la *Cosine Similarity*.

In entrambi i gruppi di soggetti è presente una buona similarità intraindividuale tra le matrici di connettività, soprattutto nelle bande di frequenza theta e beta. Nel gruppo ADHD non sembrano riconoscibili patterns di connettività generalizzabili in tutte le bande considerate, anche se la costanza intraindividuale sembra meno definita rispetto ai controlli.

I dati preliminari dello studio suggeriscono la possibile presenza di patterns di connettività del sonno riproducibili all'interno dello stesso soggetto.

## 335 - ANALISI FUNZIONALE DEI PROCESSI COGNITIVI NELL'ADHD

**G. Vannini, F. Venditti**

ASL 10, Firenze

Per una più chiara diagnosi dell'ADHD, il DSM V suggerisce di prendere in considerazione le manifestazioni cognitive. La teoria PASS ridefinisce il concetto di intelligenza umana attraverso un approccio multidimensionale. In questa luce, gli obiettivi del presente studio saranno quelli di verificare: a) se le debolezze nei processi di pianificazione e di attenzione sono presenti; b) se la teoria PASS potrebbe essere utile nella diagnosi differenziale dei tre sottotipi di ADHD; c) l'indipendenza del QI dai processi PASS.

20 soggetti, di età compresa fra i 6 e i 12 anni, sono stati valutati con il CAS e con la WISC-IV.

I profili CAS mostrano che i soggetti hanno più bassi punteggi nei processi di Pianificazione e di Attenzione. Inoltre, dalla valutazione del QI emerge un profilo medio, mentre i profili CAS differiscono leggermente tra i soggetti.

I dati indicano che i soggetti affetti da ADHD potrebbero avere qualche debolezza nei processi cognitivi di pianificazione e di attenzione. I risultati sembrano fornire alcune indicazioni circa il potenziale del CAS di trovare un particolare profilo cognitivo per i soggetti con tale diagnosi e un potere promettente nella differenziazione dei tre sottotipi di ADHD.

### **324 - VALUTAZIONE DEI NEUROLOGICAL SOFT SIGNS E DELLE FUNZIONI ESECUTIVE NEI BAMBINI CON DISTURBO DA DEFICIT DI ATTENZIONE CON IPERATTIVITÀ (ADHD), AUTISMO AD ALTO FUNZIONAMENTO (HFA) E LORO COMORBIDITÀ**

**M. Pitzianti, E. D'Agati, M. Pontis, A. Baratta, P. Curatolo, A. Pasini**

*Unità Operativa Complessa di Neuropsichiatria Infantile Policlinico Tor Vergata di Roma*

Nell'ADHD e nell'HFA sono comunemente riscontrabili deficit delle funzioni esecutive (FE) ed anomalie motorie come i *neurological soft signs* (NSS). Pertanto la valutazione del funzionamento esecutivo e motorio nei bambini *drug-naive* affetti da uno o da entrambi i disturbi può essere di fondamentale importanza per comprendere e differenziare i substrati biologici ed i fenotipi neurocognitivi associati a questi disordini del neurosviluppo. Scopo dello studio è stato confrontare le prestazioni di pazienti e controlli su compiti motori, di pianificazione, inibizione della risposta e *working memory* (WM).

Sono stati esaminati 13 soggetti con ADHD, 13 con HFA, 12 con ADHD+HFA e 13 controlli, di età compresa tra 8 e 15 anni e con quoziente intellettivo  $\geq 85$ , utilizzando una batteria completa per la valutazione delle FE e dei NSS (*overflow movements*-OM, disritmia e velocità di esecuzione dei movimenti a tempo).

I gruppi clinici hanno mostrato deficit delle FE ed un gran numero di NSS rispetto ai controlli. Il gruppo "ADHD" ha esibito maggiori deficit di pianificazione e WM ed un numero maggiore di OM rispetto al gruppo "HFA". Il gruppo "ADHD+HFA" ha presentato maggiori deficit di pianificazione rispetto agli altri gruppi clinici.

La compromissione di pianificazione e WM e la persistenza degli OM differenziano il gruppo "ADHD" rispetto al gruppo "HFA" ed ai controlli. Infine, una più severa compromissione della pianificazione è caratteristica del gruppo "ADHD+HFA".

Per ricevere la newsletter iscriversi al seguente indirizzo:

<http://crc.marionegri.it/bonati/adhdnews/subscribe.html>

Iniziativa nell'ambito del Progetto di Neuropsichiatria dell'Infanzia e dell'Adolescenza  
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Capofila Progetto: UONPIA Azienda Ospedaliera "Spedali Civili di Brescia"  
"Percorsi diagnostico-terapeutici per l'ADHD".