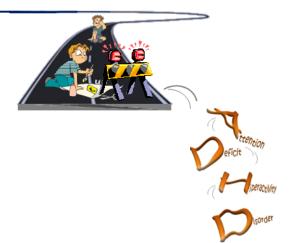
## **NEWSLETTER**





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Oliva F, et al.		
BIPOLAR DISORDER IN ADHD: FREQUENT COMORBIDITY OR SEVERE NEURODEVELOPMENTAL DISORDER?		
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## **BIBLIOGRAFIA ADHD LUGLIO 2018**

Acta Neurol Belg. 2018;1-7.

ATTENTION-DEFICIT HYPERACTIVITY DISORDER IN BRAZILIAN PATIENTS WITH PHENYLKETONURIA. da Silva FGS, Vairo E, de Souza CFM, et al.

Recent studies have shown that patients with phenylketonuria (PKU), even with the early diagnosis and continuous treatment, may have symptoms of attention-deficit hyperactivity disorder (ADHD) and that the prevalence of ADHD in this population would be higher than in the general population. This study aims to determine the prevalence of ADHD in a sample of PKU patients from Southern Brazil. Patients were prospectively assessed by clinical interviews, neurological examination, and application of the MTA-SNAP-IV scales for patients aged  $5\Gamma$ Çô17 years and the Adult Self-Report Scale for patients over 17 years. Thirty-one patients (mean age = 17.4; early diagnosis = 27) were followed. Patients with ADHD and younger than 17 years had a median Phe in the last 6 months of life higher than those without the diagnosis of ADHD (ADHD patients = 617.1 -Ámol/L, no-ADHD patients 393.2 -Ámol/L, and p = 0.03). There was a predominantly hyperactive/impulsivity clinical presentation of ADHD (n = 4/5 patients), which differs from that reported elsewhere in the literature. Future studies are essential to better define the clinical presentation of ADHD in these patients and further elucidate its pathophysiology

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Per la ricerca degli articoli pubblicati nella letteratura scientifica nel mese in esame sono state consultate le banche dati Medline, Embase, PsycINFO e PsycArticle utilizzando le seguenti parole chiave (o i loro sinonimi): 'Attention deficit disorder', 'Attention deficit hyperactivity disorder', 'Infant', 'Child', 'Adolescent', 'Human'. Sono qui riportate le referenze considerate rilevanti e pertinenti.

ADHD Atten Deficit Hyperact Disord. 2017;9:219-29.

PREDICTORS OF RELAPSE OR MAINTENANCE OF RESPONSE IN PEDIATRIC AND ADULT PATIENTS WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER FOLLOWING DISCONTINUATION OF LONG-TERM TREATMENT WITH ATOMOXETINE.

Thome J, Dittmann RW, Greenhill LL, et al.

We identified relapse/maintenance-of-response (MOR) predictors following discontinuation of long-term atomoxetine treatment in pediatric and adult patients with attention-deficit/hyperactivity disorder (ADHD) and assessed correlations between ADHD symptoms and quality of life (QoL). Post hoc analyses of data from two randomized, double-blind, placebo-controlled, phase 3 withdrawal studies in patients with ADHD meeting predefined response criteria before randomization. Study 1: patients (N = 163; 6-15 years) received atomoxetine (1.2-1.8 mg/kg/day) for 1 year, followed by randomization to atomoxetine (n = 81) or placebo (n = 82) for 6 months. Study 2: patients (N = 524; 18-50 years) received atomoxetine (80-100 mg/day) for ~6 months, followed by randomization to atomoxetine (n = 266) or placebo (n = 258) for ~6 months. Placebo patients were used for the analyses. Relapse: ≥50% worsening of prerandomization improvement in ADHD symptoms and ≥2 level severity increase on the Clinical Global Impression-Severity (CGI-S) scale at 2 consecutive visits; MOR: retaining ≥75% of prerandomization symptom improvement and CGI-S ≤ 2 at all visits (study 1); retaining ≥70% of prerandomization symptom improvement and CGI-S ≤ 3 at all visits (study 2). In adults, statistically significantly (P ≤ .05) increased likelihood of relapse was associated with prerandomization presence of Conners' Adult Attention-Deficit/Hyperactivity Disorder Rating Scale-Investigator-Rated:Screening Version (CAARS-Inv:SV) items "difficulty awaiting turn" and "careless mistakes." In pediatric patients, less MOR was associated with prerandomization presence of ADHD Rating Scale-IV-Parent Version Investigator-Rated item "does not listen"; in adults, less MOR was associated with prerandomization presence of CAARS-Inv:SV items "loses things" and "difficulty awaiting turn." Changes in patients' QoL after withdrawal from atomoxetine moderately correlated with changes in ADHD symptoms in pediatric patients and mildly in adults

ADHD Atten Deficit Hyperact Disord. 2017;9:239-51.

THE RISK OF MISDIAGNOSING POSTURE WEAKNESS AS HYPERACTIVITY IN ADHD: A CASE STUDY.

#### Voat C.

Difficulties in sustaining posture can present with features associated with hyperactive behaviour listed in DSM-5 and ICD-10 classifications for ADHD. Information from a system measuring motor activity during a neurocognitive test (QbTest), occupational therapist reports and Conners rating scales are compared between cases with and without posture problems. Weakness in sustaining posture results in elevated activity measures during infrared motion analysis. Strong posture on the other hand appears to mitigate activity levels. Posture is an independent factor which requires consideration during the assessment of ADHD

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ADHD Atten Deficit Hyperact Disord. 2018;1-11.

WHAT STOPS PRACTITIONERS DISCUSSING MEDICATION BREAKS IN CHILDREN AND ADOLESCENTS WITH ADHD? IDENTIFYING BARRIERS THROUGH THEORY-DRIVEN QUALITATIVE RESEARCH.

#### Ibrahim K. Donvai P.

National and international guidelines on the treatment of attention deficit hyperactivity disorder (ADHD) in children and adolescents call for annual reviews to assess continuing need for medication by considering brief periods without medication, referred to as  $\Gamma \zeta \ddot{y}$ Drug holidays $\Gamma \zeta \ddot{o}$ . However, drug holidays are reactively initiated by families, or recommended by practitioners if growth has been suppressed by medication rather than proactively to check the need. There is little evidence of planned, practitioner-initiated drug holidays from methylphenidate. The aim of this study was to identify what stops practitioners from routinely discussing planned drug holidays from methylphenidate with children, adolescents, and their parents. Practitioners involved in shared-care prescribing for children and adolescents with ADHD in one UK County were included. Interviews with 8 general practitioners (GPs) and 8 Child and Adolescent Mental Health Service (CAMHS) practitioners were conducted. Transcripts were analysed qualitatively against the components of the

Capability Opportunity Motivation Behaviour (COM-B) model. Possible interventions for increasing prescribers \( \tilde{\text{CO}} \) engagement with planned drug holidays were considered in response. Multiple barriers to practitioner engagement in planned drug holidays from methylphenidate were identified. Capability, in terms of knowledge and skills, was not a barrier identified for CAMHS practitioners but was for GPs. Opportunity was a main barrier for both groups, who reported lack of time and the absence of educational material about drug holidays. Motivation was more complex to define, with CAMHS practitioners questioning the need for drug holidays and GPs being more accepting due to worries about long-term medication side effects as well as cost savings. Education and enablement interventions were identified as key activities targeting all three components, which could feasibly increase uptake of practitioner-initiated planned drug holidays from methylphenidate. The application of the COM-B system identified a number of key barriers to practitioner engagement with drug holidays in children and adolescents with ADHD. Accordingly, a number of interventions could be developed to facilitate change. For example, educating and training GPs about ADHD management and drug holidays, and developing a decision aid to help families make informed decisions about whether or not to implement drug holidays could be used

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Arch Dis Child. 2018.

#### MATERNAL ADHD SYMPTOMS, CHILD ADHD SYMPTOMS AND BROADER CHILD OUTCOMES.

## Efron D, Furley K, Gulenc A, et al.

**Objective**: This study investigated the associations between maternal symptoms of attention deficit hyperactivity disorder (ADHD) and child functional outcomes in a community-based sample of children with and without ADHD.

**Design and setting**: In this cohort study, children with ADHD and healthy controls were recruited through schools in Melbourne, Australia, using a combined screening (Conners 3 ADHD Index) and case confirmation (Diagnostic Interview Schedule for Children Version IV) procedure.

Patients: 117 children with ADHD and 149 control children were included in the analyses.

**Main outcome measures**: Maternal ADHD symptoms (Conners Adult ADHD Rating Scale) and child outcomes (ADHD severity, quality of life (QoL), academic competence, social-emotional functioning) were measured at a mean child age of 8.9 years.

**Results**: Mothers of children with ADHD had clinically elevated ADHD symptoms compared with mothers of control children (adjusted analysis: 18.0% vs 2.0%, P<0.001). Elevated maternal ADHD symptoms were associated with greater child ADHD symptom severity and lower QoL by maternal report for children with (severity P=0.01; QoL P=0.003) and without (severity P=0.003; QoL P=0.003) ADHD. Elevated maternal ADHD symptoms were additionally associated with increased parent-rated emotional problems, peer problems and total impairment scores in children without ADHD (all P<0.01).

**Conclusions**: Maternal ADHD symptoms are associated with increased ADHD symptom severity and reduced QoL by maternal report in offspring with or without ADHD, and have broader negative associations with emotional and social functioning in children without ADHD. In the evaluation of the referred children, maternal ADHD symptoms should be considered and referral made to adult services where indicated

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Arch Dis Child. 2018.

ATTENTION-DEFICIT/HYPERACTIVITY DISORDER: VARIATION BY SOCIOECONOMIC DEPRIVATION.

Prasad V, West J, Kendrick D, et al.

**Background**: In England, there is a discrepancy between the prevalence of attention-deficit/hyperactivity disorder (ADHD) ascertained from medical records and community surveys. There is also a lack of data on variation in recorded prevalence by deprivation and geographical region; information that is important for service development and commissioning.

**Methods**: Cohort study using data from the Clinical Practice Research Datalink comprising 5196 children and young people aged 3-17 years with ADHD and 490 016 without, in 2012.

**Results**: In 2012, the recorded prevalence of ADHD was 1.06% (95% CI 1.03 to 1.09). Prevalence in the most deprived areas was double that of the least deprived areas (prevalence rate ratio 2.58 (95% CI 2.36 to 2.83)), with a linear trend from least to most deprived areas across all regions in England.

**Conclusions**: The low prevalence of ADHD in medical records may indicate considerable underdiagnosis. Higher rates in more disadvantaged areas indicate greater need for services in those areas

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Arch Dis Child, 2018.

CHRONIC TIC DISORDERS IN CHILDREN WITH ADHD.

Poh W, Payne JM, Gulenc A, et al.

**Objective**: To examine in a community-based cohort: (1) the prevalence of chronic tic disorder (CTD) in children with attention-deficit/hyperactivity disorder (ADHD) compared with non-ADHD controls at ages 7 and 10; and (2) the additional psychiatric and functional burden of CTD in children with ADHD.

**Methods**: Children aged 6-8 years with ADHD (n=179) and controls (n=212) were recruited through 43 Victorian schools using parent and teacher screening surveys (Conners 3 ADHD Index), followed by case confirmation (Diagnostic Interview Schedule for Children-IV (DISC-IV)). CTD was identified using the DISC-IV categories chronic motor tic disorder, chronic vocal tic disorder or Tourette syndrome at baseline and 36-month follow-up. Internalising and externalising disorders, social functioning, academic performance and quality of life were also measured. Tests of proportions and independent t-tests were used to compare the ADHD+CTD group with sex-matched ADHD alone children.

**Results**: Compared with controls, children with ADHD were 4.1 (95% CI 1.1 to 14.1) times more likely to have CTD at age 7, and 5.9 (95% CI 1.6 to 17.9) times more likely at age 10. Children with ADHD+CTD experienced higher rates of internalising disorders and peer problems, and poorer quality of life than those with ADHD alone.

**Conclusions**: CTD prevalence is higher in children with ADHD compared with controls, and confers substantial additional psychiatric and functional burden. Clinicians need to consider CTD in both the initial assessment and ongoing management of children with ADHD, and address both the symptoms and the associated impairments

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Behav Brain Res. 2018 Jul;347:408-13.

GUT MICROBIOTA PROFILES IN TREATMENT-NA $\tilde{A}^-$  VE CHILDREN WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER. Jiang Hy, Zhou Yy, Zhou GI, et al.

**Backgrounds**: Although increasing evidence suggests a role for the gut microbiota in neurodevelopment, the actual structure and composition of microbiota in children with attention-deficit/hyperactivity disorder (ADHD) remain unclear.

**Methods**: Thus, the present study aimed to define the characteristics of gut microbiota in treatment-naive children with ADHD and to assess their relationship with the severity of ADHD symptoms. High-throughput pyrosequencing was used to investigate the microbiota composition in fecal matter from 51 children with ADHD and 32 healthy controls (HC).

**Results**: An operational taxonomical unit (OTU)-level analysis revealed a significant decrease in the fractional representation of Faecalibacterium in children with ADHD compared to HC. In individuals with ADHD, the abundance of Faecalibacterium was negatively associated with parental reports of ADHD symptoms. However, there was no significant difference in alpha diversity between the ADHD and control groups.

**Conclusions**: This present findings support the involvement of microbiota alteration in psychiatric diseases and Faecalibacterium may represent a potential novel marker of gut microbiota in ADHD. Future studies are needed to validate these findings and to elucidate the temporal and causal relationships between these variables

BioMed Research International. 2018;2018.

PEER INCLUSION IN INTERVENTIONS FOR CHILDREN WITH ADHD: A SYSTEMATIC REVIEW AND META-ANALYSIS.

Cordier R, Vilaysack B, Doma K, et al.

**Objective**. To assess the effectiveness of peer inclusion in interventions to improve the social functioning of children with ADHD.

**Methods**. We searched four electronic databases for randomized controlled trials and controlled quasi-experimental studies that investigated peer inclusion interventions alone or combined with pharmacological treatment. Data were collected from the included studies and methodologically assessed. Meta-analyses were conducted using a random-effects model.

**Results**. Seventeen studies met eligibility criteria. Studies investigated interventions consisting of peer involvement and peer proximity; no study included peer mediation. Most included studies had an unclear or high risk of bias regarding inadequate reporting of randomization, blinding, and control for confounders. Meta-analyses indicated improvements in pre-post measures of social functioning for participants in peer-inclusive treatment groups. Peer inclusion was advantageous compared to treatment as usual. The benefits of peer inclusion over other therapies or medication only could not be determined. Using parents as raters for outcome measurement significantly mediated the intervention effect.

**Conclusions**. The evidence to support or contest the efficacy of peer inclusion interventions for children with ADHD is lacking. Future studies need to reduce risks of bias, use appropriate sample sizes, and provide detailed results to investigate the efficacy of peer inclusion interventions for children with ADHD

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BMC Psychiatry. 2018 Feb;18:34.

ATTENTION-DEFICIT HYPERACTIVITY DISORDER AND NONSUICIDAL SELF-INJURY IN A CLINICAL SAMPLE OF ADOLESCENTS: THE ROLE OF COMORBIDITIES AND GENDER.

Balazs J, Gyori D, Horvath LO, et al.

**BACKGROUND**: The aim of the present study was to investigate the possible association between attention-deficit hyperactivity disorder (ADHD) and non-suicidal self-injury (NSSI) with special focus on the role of comorbidities and gender in a clinical sample of adolescents with both a dimensional and a categorical approach to psychopathology.

**METHODS**: Using a structured interview, the Mini International Neuropsychiatric Interview Kid and a self-rated questionnaire, the Deliberate Self-Harm Inventory, the authors examined 202 inpatient adolescents (aged: 13-18 years) in the Vadaskert Child and Adolescent Psychiatric Hospital and Outpatient Clinic, Budapest, Hungary. Descriptive statistics, Mann-Whitney U test, chi-square test and mediator model were used.

**RESULTS**: Fifty-two adolescents met full criteria for ADHD and a further 77 showed symptoms of ADHD at the subthreshold level. From the 52 adolescents diagnosed with ADHD, 35 (67.30%) had NSSI, of whom there were significantly more girls than boys, boys: n = 10 (28.60%), girls: n = 25 (71.40%) ((chi(2)(1) = 10.643 p < .001 varphi = .452). Multiple mediation analyses resulted in a moderated mediation model in which the relationship between symptoms of ADHD and the prevalence of current NSSI was fully mediated by the symptoms of comorbid conditions in both sex. Significant mediators were the symptoms of affective and psychotic disorders and suicidality in both sexes and the symptoms of alcohol abuse/dependence disorders in girls.

**CONCLUSIONS**: ADHD symptoms are associated with an increased risk of NSSI in adolescents, especially in the case of girls. Our findings suggest that clinicians should routinely screen for the symptoms of ADHD and comorbidity, with a special focus on the symptoms of affective disorders and alcohol abuse/dependence psychotic symptoms to prevent NSSI

Brain Inj. 2017;31:1479-85.

ATTENTION-DEFICIT/HYPERACTIVITY DISORDER IS ASSOCIATED WITH BASELINE CHILD SPORT CONCUSSION ASSESSMENT TOOL THIRD EDITION SCORES IN CHILD HOCKEY PLAYERS.

Collings LJ, Cook NE, Porter S, et al.

**Objectives**: The objectives of this study were to report baseline, preseason data for the Child-SCAT3, stratified by attention deficit hyperactivity disorder (ADHD) status, and examine group differences in Child-SCAT3 performance between children with and without ADHD. Design: Cross-sectional study.

**Methods**: Young male hockey players (n-á=-á304), aged 8 12-years, were administered the Child-SCAT3 during pre-season. Child-SCAT3 measures included a 20-item symptom scale, a Standardised Assessment of Concussion Child Version (SAC-C), a modified Balance Error Scoring System (m-BESS), a tandem gait task, and a coordination test.

**Results**: Children with ADHD (n-á=-á20) endorsed significantly more symptoms (d-á=-á0.95) and greater symptom severity (d-á=-á1.13) compared to children without ADHD. No statistically significant differences were found between groups on Child-SCAT3 measures of cognitive or physical functioning (e.g. balance and coordination).

**Conclusions**: ADHD should be considered when interpreting Child-SCAT3 scores, especially symptom reporting, in the context of concussion assessment. Better understanding of symptom reporting in uninjured child athletes with ADHD can inform the clinical interpretation of symptoms at baseline and following an actual or suspected concussion. Normative data for the Child-SCAT3 that is not stratified by or otherwise accounts for ADHD status should be used with caution when appraising performance of children with ADHD

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Brain Sciences. 2018;8.

## MATERNAL BIOMARKERS OF ACETAMINOPHEN USE AND OFFSPRING ATTENTION DEFICIT HYPERACTIVITY DISORDER. Ji Y, Riley AW, Lee L-C, et al.

Previous studies have suggested a positive association between self-reported maternal acetaminophen use during pregnancy and risk of attention deficit hyperactivity disorder (ADHD) in offspring. We sought to examine the prospective association between maternal plasma biomarkers of acetaminophen intake and ADHD diagnosis in the offspring. This report analyzed 1180 children enrolled at birth and followed prospectively as part of the Boston Birth Cohort, including 188 with ADHD diagnosis based on electronic medical record review. Maternal biomarkers of acetaminophen intake were measured in plasma samples obtained within  $1\Gamma$ Çô3 days postpartum. Odds ratios for having ADHD diagnosis or other developmental disorders were estimated using multinomial logistic regression models, adjusting for pertinent covariables. Compared to neurotypical children, we observed significant positive dose-responsive associations with ADHD diagnosis for each maternal acetaminophen biomarker. These doseΓCôresponsive associations persisted after adjusting for indication of acetaminophen use and other pertinent covariates; and were specific to ADHD, rather than other neurodevelopmental disorders. In the stratified analyses, differential point estimates of the associations were observed across some strata of covariates. However, these differences were not statistically significant. Maternal acetaminophen biomarkers were specifically associated with increased risk of ADHD diagnosis in offspring. Additional clinical and mechanistic investigations are warranted

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Brain, Behavior, and Immunity. 2016;57:e16.

ESSENTIAL FATTY ACIDS INTAKE ASSOCIATED WITH DELAY AVERSION AND TEMPORAL PROCESSING IN CHILDREN WITH ATTENTION DEFICIT HYPERAC-TIVITY DISORDER (ADHD).

Chang J, Jingling L, Huang Y, et al.

The aim of the study is to investigate the association between intake of fatty acids, or omega-3 polyunsaturated fatty acids (n3-PUFAs), and cognitive functions in children with attention deficit hyperactivity disorder (ADHD). Twenty-one drug-na+\*ve children diagnosed with DSM-IV ADHD, and 21 non-ADHD controls were enrolled in the study. The parents were asked to record the n3-PUFAs diet intake of their

children by using the Food Frequency Questionnaire. Essential fatty acid (EFA) deficiency severity of the children was defined by the EFA deficiency scale scores. The children were also assessed by cognitive tasks, including Go-No-Go Task, Delayed Reaction Time Task, and Finger Tapping Task for inhibitory control, delay aversion, and temporal processing. The findings showed that the ADHD group had a greater severity in EFA deficiency (7.24+4.56, p =.02), and poorer performance in delay aversion (-177.88+280.40, p =.02) and temporal processing (85.34+10.96, p <.001). Moreover, ADHD symptom severity was negatively correlated with EFA deficiency. EFA deficiency was also associated with a higher delay aversion (p <.001) in this study. In conclusion, children with ADHD had a higher deficiency of EFA, and EFA deficiency had a positive association with ADHD severity and delay aversion

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Braz Oral Res. 2018 Jun;32:e52.

# DENTAL CARIES IN SCHOOLCHILDREN: INFLUENCE OF INATTENTION, HYPERACTIVITY AND EXECUTIVE FUNCTIONS. *Mota-Veloso I, Ramos-Jorge ML, Homem MA, et al.*

Attention-deficit/hyperactivity disorder (ADHD) is characterized by inappropriate levels of hyperactivity, impulsivity, and/or inattention. Individuals with ADHD may present limitations with regard to executive functions and performing activities that involve planning and/or attention/concentration. The aim of the study was to investigate the association between dental caries and signs of ADHD in a representative sample of schoolchildren. A representative sample of 851 schoolchildren aged seven to 12 years was randomly selected from public and private schools. Data acquisition involved a clinical dental examination for cavitated permanent and deciduous teeth using the DMFT/dmft indices. Neuropsychological evaluations, including the assessment of intelligence (Raven's Colored Progressive Matrix Test) and executive functions (Corsi Tapping Blocks tests and Digit Span test) were also performed. Parents/caregivers and teachers answered the SNAP-IV Questionnaire for the investigation of signs of inattention and hyperactivity in the family and school environment. Parents/caregivers also answered questionnaires addressing socioeconomic and sociodemographic characteristics. Descriptive analysis of the variables and Poisson regression with robust variance were performed. Parental reports of signs of inattention (PR: 1.28; p < 0.05) and hyperactivity (PR: 1.15: p < 0.05) were associated with a greater occurrence of caries. A better performance on the backward order of the Corsi Tapping Blocks tests (PR: 0.94; p < 0.05) and higher level of mother's schooling were associated with a lower frequency of caries. A better performance on executive function tasks was a protective factor against dental caries, whereas children considered inattentive and/or hyperactive by their parents had a higher prevalence rate of dental caries

Br J Psychiatry. 2017;211:359-64.

HIGH INTELLIGENCE AND THE RISK OF ADHD AND OTHER PSYCHOPATHOLOGY.

## Rommelse N, Antshel K, Smeets S, et al.

**Background**: High intelligence may be associated with positive (adaptive, desired) outcomes, but may also come with disadvantages. Aims: To contribute empirically to the debate concerning whether a trade-off in IQ scores exists in relation to attention-deficit hyperactivity disorder (ADHD) and related problems, suggesting that high intelligence - like low intelligence - increases the risk of ADHD.

**Method**: Curves of the relation between IQ score and ADHD problems were fitted to questionnaire data (parent, teacher, self-report) in a population-based study of 2221 children and adolescents aged 10-12 years. Externalising and internalising problems were included for comparison purposes.

**Results**: Higher IQ score was most strongly related to fewer attention problems, with more rater discrepancy in the high v. average IQ range. Attention problems - but only minimally hyperactivity/impulsivity problems - predicted functional impairment at school, also in the higher IQ range.

**Conclusions**: Attention problems in highly intelligent children are exceptional and affect school performance; they are therefore a reason for clinical concern

Cardiol Young. 2018;28:S170-S171.

ASSESSMENT OF CARDIAC FUNCTIONS, AORTIC STIFFNESS AND HEART RATE VARIABILITY PARAMETERS IN CHILDREN WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER.

#### Gurses D, Kizilkaya A, et al.

**Introduction**: Attention deficit hyperactivity disorder (ADHD) is characterized by decreased attention span, impulsiveness, and hyperactivity. Cardiovascular involvement can be seen secondary to autonomic dysfunction. This study is conducted in order to assess possible cardiac involvement in children with ADHD and whether we investigate differences in ADHD subtypes or not.

**Methods**: In this cross-sectional study, we evaluated 73 children with ADHD (14 with hyperactivity, 25 with inattentive, and 35 with combined type), and 37 healthy children as controls. Cardiac evaluation was made using an electrocardiogram, conventional and tissue Doppler echocardiography and ambulatory holtermonitoring.

**Results**: Systolic blood pressure and mean heart rate increased in ADHD patients (p< 0.05). QT and QTc dispersion, which show ventricular repolarization homogeneity were similar in the groups (p >0.05). Left ventricle Sdm, Edm/Adm and interventricular septum Edivs/Adivs decreased by the measurements made by tissue Doppler echocardiography in ADHD patients (p< 0.05). Aortic stiffness parameters were found similar in the two groups (p >0.05). SDNN, rMSSD and pNN50 decreased in the children with ADHD (p <0.01). As compared within ADHD subtypes; heart rate was higher, pNN50 and RMSSD were lower in combined subtype than the other subtypes (p <0.01).

**Conclusions**: Our findings showed cardiac involvement can exist in ADHD patients as secondary to autonomic dysfunction. This involvement was higher in combined subtype. Children with ADHD were at risk for cardiovascular complication. Before treatment, assessing all children with ADHD, especially combined subtype using with ambulatory Holter monitoring and tissue Doppler echocardiography in addition to detailed physical examination and electrocardiography might be helpful to detect cardiac complication in preclinical stage of the cardiac involvement

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Clin Case Stud. 2018:17:207-19.

COMORBID HOARDING AND OBSESSIVE COMPULSIVE DISORDER MANIFESTED DURING EARLY CHILDHOOD.

### Borda T, Gardini DH, Neziroglu F.

This case report outlines the use of cognitive behavioral therapy (CBT) used to treat an 11-year-old female, Gabriela, with comorbid hoarding and obsessive compulsive disorder (OCD). Gabriela participated in treatment involving CBT and exposure and response prevention (ERP) sessions for OCD and hoarding, following a cognitive rehabilitation software program designed for cognitive impairment. Upon completion of the treatment, Gabriela no longer exhibited behaviors consistent with a comorbid hoarding and OCD diagnosis and demonstrated marked improvements in her presenting problems (mental rituals; hoarding items for magical thinking purposes). This case report supports the focus of research, continuing to explore hoarding and comorbidity diagnoses across the life span

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Clin EEG Neurosci, 2018.

PREDICTING CLINICAL GAINS AND SIDE EFFECTS OF STIMULANT MEDICATION IN PEDIATRIC ATTENTION-DEFICIT/HYPERACTIVITY DISORDER BY COMBINING MEASURES FROM QEEG AND ERPS IN A CUED GO/NOGO TASK.

## Ogrim G, Kropotov JD.

**Objectives**. The study aim was to develop 2 scales: predicting clinical gains and risk of acute side effects of stimulant medication in pediatric attention-deficit/hyperactivity disorder (ADHD), combining measures from EEG spectra, event-related potentials (ERPs), and a cued visual GO/NOGO task.

**Methods**. Based on 4-week systematic medication trials, 87 ADHD patients aged 8 to 17 years were classified as responders (REs, n = 62) or non-REs (n = 25), and belonging to the side effects (SEs, n = 42) or no-SEs (n = 45) groups. Before starting the trial, a 19-channel EEG was registered twice: Test 1 (T1)

without medication and T2 on a single dose of stimulant medication a few days before the trial. EEG was registered T1 and T2: 3 minutes eyes-closed, 3 minutes eyes-open, and 20 minutes cued GO/NOGO. EEG spectra, ERPs, omissions, commissions, reaction time (RT), and RT variability were computed. Groups were compared at T1 and T2 on quantitative EEG (qEEG), ERPs and behavioral parameters; effect sizes (d) were estimated. Variables with d > 0.5 were converted to quartiles, multiplied by corresponding d, and summed to obtain 2 global scales.

**Results.** Six variables differed significantly between REs and non-REs (T1: theta/alpha ratio, P3NOGO amplitude. Differences T2-T1: Omissions, RT variability, P3NOGO, contingent negative variation [CNV]). The global scale d was 1.86. Accuracy (receiver operating characteristic) was 0.92. SEs and no-SEs differed significantly on 4 variables. (T1: RT, T2: novelty component and alpha peak frequency, and RT changes. Global scale d = 1.08 and accuracy = 0.78.

**Conclusion**. Gains and side effects of stimulants in pediatric ADHD can be predicted with high accuracy by combining EEG spectra, ERPs, and behavior from baseline and single-dose tests. ClinicalTrials.gov identifier: NCT02695355

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Clin Pediatr. 2018.

SCREENING FOR ATTENTION-DEFICIT/HYPERACTIVITY DISORDER AND COMORBIDITIES IN A DIVERSE, URBAN PRIMARY CARE SETTING.

### Spencer AE, Plasencia N, Sun Y, et al.

We tested the accuracy of 2 parent-report tools, the Pediatric Symptom Checklist (PSC-35) and Child Behavior Checklist (CBCL), to identify attention-deficit/hyperactivity disorder (ADHD) and distinguish complex (highly comorbid) cases in an urban, largely Latino pediatric practice. Spanish- and English-speaking parents of children aged 6 to 10 years completed a PSC-35 and CBCL at well visits. Those with CBCL Attention Problems Subscale (CBCL-APS) T scores ΓέÑ60 plus controls completed the diagnostic MINI-KID (Miniature International Neuropsychiatric Interview) for Children. Receiver operating characteristic (ROC) curves quantified accuracy of both scales to distinguish ADHD from non-ADHD, and complex from simple ADHD. Two hundred and nine children were screened, and 41 completed diagnostic interviews. Both the CBCL-APS and PSC Attention Scale (PSC-AS) accurately identified ADHD; the CBCL-APS performed best (AUROCCBCL\_APS = 0.837; AUROCPSC\_AS = 0.728). The PSC Total and Internalizing Scores and the number of CBCL subscale elevations accurately distinguished complex from simple ADHD; the PSC Internalizing Score performed best (AUROCPSC\_TOTAL = 0.700; AUROCPSC\_INT = 0.817; AUROCCBCL\_SUBS = 0.762)

Cochrane Database Syst Rev. 2018 May:5:CD012069.

METHYLPHENIDATE FOR ATTENTION DEFICIT HYPERACTIVITY DISORDER (ADHD) IN CHILDREN AND ADOLESCENTS - ASSESSMENT OF ADVERSE EVENTS IN NON-RANDOMISED STUDIES.

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Storebo OJ, Pedersen N, Ramstad E, et al.

**BACKGROUND**: Attention deficit hyperactivity disorder (ADHD) is a common neurodevelopmental disorder in childhood. The psychostimulant methylphenidate is the most frequently used medication to treat it. Several studies have investigated the benefits of methylphenidate, showing possible favourable effects on ADHD symptoms, but the true magnitude of the effect is unknown. Concerning adverse events associated with the treatment, our systematic review of randomised clinical trials (RCTs) demonstrated no increase in serious adverse events, but a high proportion of participants suffered a range of non-serious adverse events.

**OBJECTIVES**: To assess the adverse events associated with methylphenidate treatment for children and adolescents with ADHD in non-randomised studies.

**SEARCH METHODS**: In January 2016, we searched CENTRAL, MEDLINE, Embase, PsycINFO, CINAHL, 12 other databases and two trials registers. We also checked reference lists and contacted authors and pharmaceutical companies to identify additional studies.

**SELECTION CRITERIA**: We included non-randomised study designs. These comprised comparative and non-comparative cohort studies, patient-control studies, patient reports/series and cross-sectional studies of methylphenidate administered at any dosage or formulation. We also included methylphenidate groups from RCTs assessing methylphenidate versus other interventions for ADHD as well as data from follow-up periods in RCTs. Participants had to have an ADHD diagnosis (from the 3rd to the 5th edition of the Diagnostic and Statistical Manual of Mental Disorders or the 9th or 10th edition of theInternational Classification of Diseases, with or without comorbid diagnoses. We required that at least 75% of participants had a normal intellectual capacity (intelligence quotient of more than 70 points) and were aged below 20 years. We excluded studies that used another ADHD drug as a co-intervention.

DATA COLLECTION AND ANALYSIS: Fourteen review authors selected studies independently. Two review authors assessed risk of bias independently using the ROBINS-I tool for assessing risk of bias in non-randomised studies of interventions. All review authors extracted data. We defined serious adverse events according to the International Committee of Harmonization as any lethal, life-threatening or life-changing event. We considered all other adverse events to be non-serious adverse events and conducted meta-analyses of data from comparative studies. We calculated meta-analytic estimates of prevalence from non-comparative cohorts studies and synthesised data from patient reports/series qualitatively. We investigated heterogeneity by conducting subgroup analyses, and we also conducted sensitivity analyses. MAIN

**RESULTS**: We included a total of 260 studies: 7 comparative cohort studies, 6 of which compared 968 patients who were exposed to methylphenidate to 166 controls, and 1 which assessed 1224 patients that were exposed or not exposed to methylphenidate during different time periods; 4 patient-control studies (53,192 exposed to methylphenidate and 19,906 controls); 177 non-comparative cohort studies (2,207,751 participants); 2 cross-sectional studies (96 participants) and 70 patient reports/series (206 participants). Participants' ages ranged from 3 years to 20 years. Risk of bias in the included comparative studies ranged from moderate to critical, with most studies showing critical risk of bias. We evaluated all non-comparative studies at critical risk of bias. The GRADE quality rating of the evidence was very low. Primary outcomes In the comparative studies, methylphenidate increased the risk ratio (RR) of serious adverse events (RR 1.36, 95% confidence interval (CI) 1.17 to 1.57; 2 studies, 72,005 participants); any psychotic disorder (RR 1.36, 95% CI 1.17 to 1.57; 1 study, 71,771 participants); and arrhythmia (RR 1.61, 95% CI 1.48 to 1.74; 1 study, 1224 participants) compared to no intervention. In the non-comparative cohort studies, the proportion of participants on methylphenidate experiencing any serious adverse event was 1.20% (95% CI 0.70% to 2.00%; 50 studies, 162,422 participants). Withdrawal from methylphenidate due to any serious adverse events occurred in 1.20% (95% CI 0.60% to 2.30%; 7 studies, 1173 participants) and adverse events of unknown severity led to withdrawal in 7.30% of participants (95% CI 5.30% to 10.0%; 22 studies, 3708 participants). Secondary outcomes In the comparative studies, methylphenidate, compared to no intervention, increased the RR of insomnia and sleep problems (RR 2.58, 95% CI 1.24 to 5.34; 3 studies, 425 participants) and decreased appetite (RR 15.06, 95% CI 2.12 to 106.83; 1 study, 335 participants). With non-comparative cohort studies, the proportion of participants on methylphenidate with any non-serious adverse events was 51.2% (95% CI 41.2% to 61.1%; 49 studies, 13,978 participants). These included difficulty falling asleep, 17.9% (95% CI 14.7% to 21.6%; 82 studies, 11,507 participants); headache, 14.4% (95% CI 11.3% to 18.3%; 90 studies, 13,469 participants); abdominal pain, 10.7% (95% CI 8.60% to 13.3%; 79 studies, 11,750 participants); and decreased appetite, 31.1% (95% CI 26.5% to 36.2%; 84 studies, 11,594 participants). Withdrawal of methylphenidate due to non-serious adverse events occurred in 6.20% (95% CI 4.80% to 7.90%; 37 studies, 7142 participants), and 16.2% were withdrawn for unknown reasons (95% CI 13.0% to 19.9%; 57 studies, 8340 participants).

**AUTHORS' CONCLUSIONS**: Our findings suggest that methylphenidate may be associated with a number of serious adverse events as well as a large number of non-serious adverse events in children and adolescents, which often lead to withdrawal of methylphenidate. Our certainty in the evidence is very low, and accordingly, it is not possible to accurately estimate the actual risk of adverse events. It might be higher than reported here. Given the possible association between methylphenidate and the adverse events identified, it may be important to identify people who are most susceptible to adverse events. To do this we must undertake large-scale, high-quality RCTs, along with studies aimed at identifying responders and non-responders

Cogn Behav Pract. 2018.

MANAGING FRUSTRATION FOR CHILDREN (MFC) GROUP INTERVENTION FOR ADHD: AN OPEN TRIAL OF A NOVEL GROUP INTERVENTION FOR DEFICIENT EMOTION REGULATION.

Rosen PJ, Leaberry KD, Slaughter K, et al.

Deficient emotion regulation is a common and impairing area of difficulty among children with ADHD. Few interventions specifically address deficient emotion regulation. The Managing Frustration for Children With ADHD (MFC) group treatment was developed to specifically target deficient emotion regulation deficits common to children with ADHD. The MFC was developed as a 12-week multisystemic intervention for emotion regulation deficits among children with ADHD. An open trial assessed the effectiveness of the MFC as an adjunctive treatment for deficient emotion regulation among children with ADHD. Fifty-two children with ADHD ages 9FÇô11 (42 boys, 10 girls) were enrolled in the MFC, with 44 completing treatment. The majority (71.2%) of participants had at least one comorbid internalizing, externalizing, or learning disorder. Intent-to-treat repeated-measures ANCOVA suggested significant decreases in emotion regulation deficits, mood difficulties, and externalizing difficulties following completion of treatment. More than half (53%) of children who completed treatment experienced reliable and clinically significant improvement in at least one area of functioning. The MFC demonstrated promising initial effectiveness in addressing the emotion regulation deficits of children with ADHD

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Cortex. 2018;106:164-73.

WAITING AND WORKING FOR REWARDS: ATTENTION-DEFICIT/HYPERACTIVITY DISORDER IS ASSOCIATED WITH STEEPER DELAY DISCOUNTING LINKED TO AMYGDALA ACTIVATION, BUT NOT WITH STEEPER EFFORT DISCOUNTING. Mies GW, Ma I, De WE, et al.

**Objective**: Children and adolescents with ADHD have a relatively strong preference for smaller immediate rewards over larger delayed rewards (steep delay discounting). It is unknown whether such steep discounting of rewards is specific for delayed rewards, i.e., supporting the delay aversion account of ADHD, or whether it is also present for effortful rewards, i.e., representing general reward insensitivity. Therefore, this study examined behavioral and BOLD responses during delay discounting (DD) and effort discounting (ED) in ADHD.

**Method**: Thirty adolescents with ADHD and 28 controls ( $12\Gamma$ Çô17 years) were scanned while performing a DD-ED task (fMRI findings were based on 21 and 25 participants, respectively). During DD, participants were presented with a series of choices between a small reward delivered immediately and a larger reward delivered after  $5\Gamma$ Çô25s. During ED, participants were presented with choices between a small reward that was delivered after exerting 15% of their maximal hand grip strength and a larger reward delivered after exerting 30-90% of their strength.

**Results**: Analyses on the subjective values of delayed and effortful rewards and on the Area Under the discounting Curves (AUCs) indicated that adolescents with ADHD showed steeper discounting than controls for DD, but not for ED. This was accompanied by a slightly stronger delay dose response relationship in the amygdala for adolescents with ADHD who reported to be more delay averse in daily life.

**Conclusion**: Together, these results steeper DD in the ADHD group and a stronger delay dose response relationship in the amygdala, while no evidence for group differences in ED was found support the delay aversion account of ADHD

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Dev Neuropsychol. 2018;43:430-53.

COGNITIVE PREDICTORS OF SEQUENTIAL MOTOR IMPAIRMENTS IN CHILDREN WITH DYSLEXIA AND/OR ATTENTION DEFICIT/HYPERACTIVITY DISORDER.

Marchand-Krynski ME, Belanger AM, Morin-Moncet O, et al.

This study examined cognitive predictors of sequential motor skills in 215 children with dyslexia and/or attention deficit/hyperactivity disorder (ADHD). Visual working memory and math fluency abilities contributed significantly to performance of sequential motor abilities in children with dyslexia (N = 67), ADHD (N = 66)

and those with a comorbid diagnosis (N = 82), generally without differentiation between groups. In addition, primary diagnostic features of each disorder, such as reading and inattention, did not contribute to the variance in motor skill performance of these children. The results support a unifying framework of motor impairment in children with neurodevelopmental disorders such as dyslexia and ADHD

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Dev Neuropsychol. 2018;43:403-18.

WHICH NEUROPSYCHOLOGICAL FUNCTIONS PREDICT VARIOUS PROCESSING SPEED COMPONENTS IN CHILDREN WITH AND WITHOUT ATTENTION-DEFICIT/HYPERACTIVITY DISORDER?

### Vadnais SA, Kibby MY, Jagger-Rickels AC.

We identified statistical predictors of four processing speed (PS) components in a sample of 151 children with and without attention-deficit/hyperactivity disorder (ADHD). Performance on perceptual speed was predicted by visual attention/short-term memory, whereas incidental learning/psychomotor speed was predicted by verbal working memory. Rapid naming was predictive of each PS component assessed, and inhibition predicted all but one task, suggesting a shared need to identify/retrieve stimuli rapidly and inhibit incorrect responding across PS components. Hence, we found both shared and unique predictors of perceptual, cognitive, and output speed, suggesting more specific terminology should be used in future research on PS in ADHD

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Dev Neuropsychol. 2018;43:419-29.

DEVELOPMENTAL TRAJECTORY OF MOTOR DEFICITS IN PRESCHOOL CHILDREN WITH ADHD.

## Sweeney KL, Ryan M, Schneider H, et al.

Motor deficits persisting into childhood (>7 years) are associated with increased executive and cognitive dysfunction, likely due to parallel neural circuitry. This study assessed the longitudinal trajectory of motor deficits in preschool children with ADHD, compared to typically developing (TD) children, in order to identify individuals at risk for anomalous neurological development. Participants included 47 children (21 ADHD, 26 TD) ages 4-7 years who participated in three visits (V1, V2, V3), each one year apart (V1=48-71 months, V2=60-83 months, V3=72-95 months). Motor variables assessed included speed (finger tapping and sequencing), total overflow, and axial movements from the Revised Physical and Neurological Examination for Subtle Signs (PANESS). Effects for group, visit, and group-by-visit interaction were examined. There were significant effects for group (favoring TD) for finger tapping speed and total axial movements, visit (performance improving with age for all 4 variables), and a significant group-by-visit interaction for finger tapping speed. Motor speed (repetitive finger tapping) and quality of axial movements are sensitive markers of anomalous motor development associated with ADHD in children as young as 4 years. Conversely, motor overflow and finger sequencing speed may be less sensitive in preschool, due to ongoing wide variations in attainment of these milestones

Developmental Medicine & Child Neurology. 2018 Jul;60:711-17.

HEALTH RELATED QUALITY OF LIFE AND PEER RELATIONSHIPS IN ADOLESCENTS WITH DEVELOPMENTAL COORDINATION DISORDER AND ATTENTION DEFICIT HYPERACTIVITY DISORDER.

## Dewey D, Volkovinskaia A.

**AIM**: Health-related quality of life (HRQoL) and peer relationships were investigated in adolescents with developmental coordination disorder (DCD) and attention-deficit-hyperactivity disorder (ADHD).

**METHOD**: Adolescents with DCD (n=9), ADHD (n=9), DCD and ADHD (n=10), and typically developing adolescents (n=16) completed the following questionnaires: KIDSCREEN-52 Health-Related Quality of Life

Questionnaire and Peer Relations Questionnaire for Children. Twenty-five participants took part in semistructured interviews.

**RESULTS**: Adolescents with DCD and ADHD had lower HRQoL on the mood and emotions, school environment, and financial resources scales of the KIDSCREEN-52 than adolescents in the DCD and typically developing groups (all p<0.05). On the Peer Relations Questionnaire for Children, the DCD and ADHD group reported significantly higher victimization compared with those in the typically developing (p=0.030) and DCD (p=0.010) groups. Qualitative interviews among young people with DCD and ADHD revealed feelings of marginalization and victimization. Descriptors such as 'misfits', 'oddballs', 'weird', and 'the rejects' were used to describe themselves.

**INTERPRETATION**: HRQoL and peer relationships are negatively affected in adolescents with DCD and ADHD. WHAT THIS PAPER ADDS?: Children with developmental coordination disorder (DCD) do not display poorer overall health-related quality of life (HRQoL) versus typically developing controls. Having DCD and attention-deficit-hyperactivity disorder (ADHD) was associated with poorer HRQoL. Adolescents with DCD and ADHD experience significantly higher levels of peer victimization than typically developing adolescents. HRQoL and peer relationships are significantly associated in adolescent respondents

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Diabetes Care. 2018 Apr;41:770-74.

Type 1 Diabetes in Parents and Risk of Attention Deficit/Hyperactivity Disorder in Offspring: A Population-Based Study in Sweden.

Ji J, Chen T, Sundquist J, et al.

**OBJECTIVE**: To explore whether a family history of type 1 diabetes (T1D) is associated with an increased incidence of attention deficit/hyperactivity disorder (ADHD) in offspring.

**RESEARCH DESIGN AND METHODS**: Individuals with T1D were identified from the nationwide Swedish National Hospital Discharge Register and Swedish Outpatient Register in Sweden and were linked to the Swedish Multi-Generation Register to identify their offspring. Cox regression was used to calculate the hazard ratio (HR) of ADHD in offspring of patients with T1D compared with the general population.

**RESULTS**: A total of 15,615 individuals were born after their parents were diagnosed with T1D. After a set of confounding factors was controlled for, offspring of T1D patients had a significantly increased risk of ADHD with an HR of 1.29 (95% CI 1.15-1.42). Maternal T1D was associated with an enhanced risk of ADHD (HR 1.35 [95% CI 1.18-1.55]) compared with paternal T1D (HR 1.20 [95% CI 1.03-1.41]), but the difference was not statistically significant.

**CONCLUSIONS**: In this retrospective cohort study, we found that a parental history of T1D was associated with a 29% increased risk of being diagnosed with ADHD. However, the underlying mechanisms need to be explored in future studies

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Environ Res. 2018:166:481-86.

ASSOCIATIONS BETWEEN URINARY COTININE AND SYMPTOMS OF ATTENTION DEFICIT/HYPERACTIVITY DISORDER AND AUTISM SPECTRUM DISORDER.

Kim KM. Lim MH. Kwon H-J. et al.

**Background**: The present study investigated associations between urinary cotinine levels as a biomarker of secondhand smoke exposure and symptoms of attention deficit/hyperactivity disorder (ADHD) and autism spectrum disorder (ASD).

**Methods**: A total of 520 child participants (200 with ADHD, 67 with ASD, and 253 normal control subjects) were assessed using the Korean version of the ADHD rating scale (K-ARS), Autism spectrum screening questionnaire (ASSQ), and Behavioral Assessment System for Children, second edition (BASC-2). The Korean version of the computer-based continuous performance test was used to assess cognitive function. Urinary cotinine was evaluated as a biomarker of secondhand smoke exposure.

**Results**: Urinary cotinine levels were significantly and positively associated with K-ARS score (B = 4.00, p < 0.001), ASSQ score (B = 1.71, p = 0.030), the behavioral problem subscales of the BASC-2 (B = 1.68-3.52,

p < 0.00-0.045), and omission and commission errors in the continuous performance test (B = 6.21-8.42, p < 0.001 $\Gamma$ Çô0.019). Urinary cotinine levels were also associated with the increased odds ratio of ADHD (OR = 1.55, 95% CI 1.05 $\Gamma$ Cô2.30, p = 0.028) and ASD (OR = 1.89, 95% CI 1.12-3.21, p = 0.018).

**Conclusion**: Urinary cotinine levels were associated with lower behavioral adaptation and cognitive function and increased odds ratios of ADHD and ASD, indicating a negative effect of secondhand smoke exposure on the symptomatic manifestation of ADHD and ASD

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Erciyes Medical Journal. 2017;39:S68.

MOLECULAR AND CYTOGENETIC CHARACTERIZATION OF CHROMOSOME 4P AND 22Q13.3 DUPLICATION IN A HYPERACTIVE 10-YEAR-OLD GIRL WITH SHORT STATURE, ATTENTION DEFICIT AND INTELLECTUAL DISABILITY.

#### Silan F, Urfali M, et al.

Department of Medical Genetics, Canakkale Onsekiz Mart University Faculty of Medicine Canakkale The chromosomal 4p duplication results in recognizable clinical findings of mental retardation and congenital anomalies. Here we present clinical, molecular and cytogenetic data on a 10-years-old girl with 4p duplication. The clinical symptoms for the current presented case were clinodactily of the fifth digit, triangular face, bicuspid aortic valve, myopia, high palate, short stature, attention deficit, intellectual disability and convulsion attacks. The chomosome dup(4p) was detected by standard cytogenetics karyotyping, MLPA and aCGH techniques. 22q13.3 duplication was detected by FISH and aCGH technique. She was diagnosed as 46,XX,der(15),t(4;15)(p15.2;p11.2), invdup(22)(q13.3) after karyotype and aCGH genotype analyses. The aCGH analysis showed arr(hg19)4p16.3-p15.2(45,882-27,428,268)x3 and arr(hg19)22q13.3(51,062,707-51,067,384)x3 profiles. Her mother was normal but father was in 46,XY,t(4;15)(p15.2;p11.1) karyotypes after peripheral lymphocyte cell cultures analysis. Here we present a case with complex t(4p;15p) and invdup(22)(q13.3) chromosomal rearrangements and some clinical findings of affected case report. Duplication ARSA gene on 22q13.3 have no significant phenotype there by deletion of the gene results OR Metachromatic leukodystrophy. On the other hand 4p duplications results various phenotypes depending on which genes including the duplicated region Results confirmed the complicated gene duplication syndrome of the intellectual disability

Eur Child Adolesc Psychiatry. 2018.

HEAD CIRCUMFERENCE AND CHILD ADHD SYMPTOMS AND COGNITIVE FUNCTIONING: RESULTS FROM A LARGE POPULATION-BASED COHORT STUDY.

#### Ferrer M, et al.

The aim of this study is to understand the association between prenatal, newborn and postnatal head circumference (HC) and preschool neurodevelopment in a large population-based birth cohort. The INMA project followed 1795 children from 12-áweeks of pregnancy to preschool years. HC measurements were carried out prospectively, and following a standardized protocol during pregnancy (12, 20 and 34-áweeks), birth, and child ages of 1ΓÇô1.5 and 4-áyears old; and z-scores were further estimated. Prenatal head growth was assessed using conditional z-scores between weeks 12ΓÇô20 and 20ΓÇô34. Several neuropsychological tests [MSCA (cognition), CPT (attention)] and behavioral rating scales [DSM-IV-ADHD, CAST (autism), CPSCS (social competence)] were carried out during the last follow-up (5-áyears old). Multivariable models adjusted for family and child characteristics were applied to analyze associations between HC and neurodevelopment. In fully adjusted models, prenatal HC and head growth showed little or no associations with the neurodevelopment outcomes. Independent associations were observed between HC z-scores at birth, 1FCô1.5-áyears and 4-áyears and MSCA global cognitive scores and DSM-IV inattention symptoms. Specifically, z-score at birth was positively associated with general cognitive scores [+1 1.22, 95% confidence interval (CI) 0.59, 1.85], and we observed a protective association with ADHD-DSM-IV total symptoms, mean ratio (MR) 0.85 (0.75, 0.96). Prenatal HC and head growth measurements gave little information about child cognitive abilities and behavior at preschool years. However, HC at birth and early childhood was positively associated with a range of neuropsychological outcomes, including protective associations with ADHD symptoms

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Eur Child Adolesc Psychiatry. 2018;1-9.

THE DEVELOPMENTAL COURSE OF INATTENTION SYMPTOMS PREDICTS ACADEMIC ACHIEVEMENT DUE TO SHARED GENETIC AETIOLOGY: A LONGITUDINAL TWIN STUDY.

## Liu C-Y, Li Y, Viding E, et al.

Symptoms of attention-deficit hyperactivity disorder, in particular inattention symptoms, are associated with academic achievement. However, whether and why the developmental course of inattention symptoms (i.e. systematic decreases or increases of symptoms with age) predicts academic achievement remains unclear. A total of 5634 twin pairs born in the UK were included in the current study. We used latent growth curve modelling to estimate the baseline level and the developmental course of inattention symptoms (assessed at ages 8, 11, 14 and 16 years) and test whether they predicted the General Certificate of Secondary Education scores (GCSE, at age 16 years). We then implemented multivariate twin modelling to determine the role of genetic and environmental factors in explaining the relationship between inattention symptoms and GCSE scores. Increasing inattention symptoms across childhood and adolescence predicted poorer GCSE scores independently of the baseline level of inattention. Genetic factors explained most of this relationship, i.e. genetic factors contributing to individual differences in the developmental course of inattention also influenced GCSE scores. In conclusion, our study demonstrates that genetic factors underlying the developmental course of inattention symptoms across childhood and adolescence also influence academic achievement. This may result from indirect mechanism, whereby genetic factors explain systematic changes in inattention levels with age, which in turn impact academic achievement. The shared genetic aetiology may also suggest common neurobiological processes underlying both the developmental course of inattention symptoms and academic achievement

Eur Neuropsychopharmacol. 2018.

VISUAL AND AUDITORY EMOTION RECOGNITION PROBLEMS AS FAMILIAL CROSS-DISORDER PHENOMENON IN ASD AND ADHD.

#### Waddington F, Hartman C, De BY, et al.

Autism spectrum disorder (ASD) and attention-deficit/hyperactivity disorder (ADHD) are frequently comorbid disorders. Emotion recognition problems are considered an important familial deficit in ASD, but this is unknown in ADHD. Very few studies have directly compared emotion recognition performance of youth with ASD and/or ADHD and of their unaffected siblings across age to quantify the contribution of emotion recognition problems to the ADHD phenotype. We therefore devised a study of 64 ASD+ADHD participants, 89 ASD-only participants, 111 ADHD-only participants, 122 unaffected ASD(+ADHD) siblings, 69 unaffected ADHD-only siblings and 220 controls aged 7ΓÇô18 years, who had completed two tasks assessing auditory and visual emotion recognition. Factor analysis was used to detect underlying dimensions of emotion recognition capacity. Linear mixed models were used to compare performance across groups and to assess age effects. The factor-analysis revealed four factors separating speed and accuracy regarding visual and auditory emotion recognition. ASD+ADHD, ASD-only, and ADHD-only participants all performed worse than controls. ASD+ADHD, ASD-only, and ADHD-only participants did not differ in the severity of their emotion recognition problems. Both unaffected sibling groups performed intermediate between patients and controls. For ASD+ADHD and ADHD-only participants, group differences were more marked in adolescence than childhood, whereas in ASD participants this was not observed. We conclude that emotion recognition problems are a familial deficit in ADHD to a similar extent as in ASD. Emotion recognition problems specifically - and social cognition problems more generally - should be assessed in clinical practice for ADHD

Eur Psychiatry. 2018;48:S471.

FREE-T3 AS A WEAKER BIOLOGICAL MARKER FOR ADHD IN ADULTS COMPARED TO CHILDREN.

## Caci H, Patricia PF, Henri I.

Introduction.- Thyroid function has been less frequently studied in adults with ADHD than in children. Some authors noticed similarities between ADHD symptoms in children and the Thyroid Hormone Resistance while others concluded that the thyroid function was normal based either on total-T3, free-T3, total-T4, free-T4 or TSH (Thyroid Stimulating Hormone). We found in a previous study that free-T3 was higher in a subgroup of children with ADHD more likely to have comorbid ODD, while free-T4 and TSH were within normal range. Objectives.- If free-T3 were a biological marker of ADHD then our findings in children would hold in a sample of adults with ADHD.

**Methods**.- Retrospective analyses of systematic biological assays performed before prescribing any psychostimulant treatment to an adult formally diagnosed with ADHD in our department since 2001.

**Results.**- No hypothyroidism or hyperthyroidism case in our sample of 83 adults (including 44 women). Biological laboratories either used IECL/Centaur or EIA/Beckman techniques. Age and free-T3 correlated (rho = -.42, P< 0001). Three adults (3.62%) had free-T3 levels beyond the reference interval provided on result sheets. Free-T3 dosage was beyond the percentile 90 of the reference interval in 8 cases out of 26 with EICL/Centaur (30.77%; p<.003 by binomial law) and beyond the percentile 95 in 6 cases out of 57 with EIA/Beckman (10.53%; p<.065).

**Conclusions.**- Those proportions are smaller than those obtained in a sample of children; one reason may be the strong negative correlation between free-T3 and age. Analyses should be replicated in a multicentre prospective and controlled study

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Eur Psychiatry. 2018;48:S246.

PREVALENCE OF ATTENTION DEFICIT HYPERACTIVITY DISORDER (ADHD) IN A PEDIATRIC ENDOCRINE CLINIC IN SAUDI ARABIA.

Habis S, Alhaidar F, Alharbi A, et al.

**Background.**- Attention-deficit hyperactivity disorder (ADHD) is a chronic neurobehavioral disorder with a substantial lifelong impact on personal and social functioning, academic performance, and the health system in general. It is one of the most frequent childhoodonset psychiatric conditions, with an estimated worldwide-pooled prevalence exceeding 5% in school-age children, and a prevalence of 1.3-16% in Arab countries. It was previously hypothesized that ADHD may be associated with hormonal changes. We aimed to address this association in the study group.

**Methods.**- This is a quantitative cross-sectional study to estimate the prevalence of ADHD among children with Endocrine disorders who attended the Pediatric Endocrine clinic at King Khalid University Hospital, Riyadh, Saudi Arabia (November 2015-March 2016). The data was gathered by an interview answering questions about social demographics, basic medical profile including the endocrine diagnosis, and a valid screening tool for ADHD (ADHD Rating Scale).

**Results.**- The study showed that ADHD was associated with low socioeconomic status and other social demographic characteristics in our study group. Analysis revealed that the prevalence of ADHDwas 14.9% (n = 46/309 children). Of these, 67.39% (n = 31/309) were males. There was no statistical evidence suggesting association between ADHD and obesity, thyroid dysfunction, and growth deficit. However, there might be an association with diabetes (Tables 1-3).

**Conclusion.**- According to our findings, ADHD may not be associated with other endocrine disorders; diabetic children are probably less likely to develop ADHD. Further larger studies are required to confirm and possibly explore potential protective mechanisms of diabetes against ADHD. (Table Presented)

Eur Psychiatry. 2018;48:S385-S386.

IMPULSIVITY, EMOTIONAL DYSREGULATION AND BIPOLAR SPECTRUM IN ADOLESCENTS. EVOLUTION AND TREATMENT IN ONE ADOLESCENT WITH COMORBIDITY BETWEEN ODD, ADHD, IMPULSIVITY, EMOTIONAL DYSREGULATION AND BIPOLAR SPECTRUM.

#### Vargas CA, Servaye J.

**Introduction.**- The irritability and Emotional Dysregulation are causes of consulting that increase day by day in our services of Child & Adolescent Mental Health. This irritability and impulsivity dysfunctional in adolescents, must be studied in their overall states.

**Background.**- There is a high comorbidity between the impulsivity, frequent irritability, outburst of anger, inattention, hyperactivity and greater degree of oppositional defiant behaviour seen in Externalizing disorders, and Bipolar Spectrum or Bipolar disorder(BD), being a challenge to diagnosis and treatment in adolescents.

**Objective.**- Demostrate by reviewing a case, the diagnostic comorbidity between Oppositional Defiant Disorder (ODD), Externalizing Disorders, Attention Deficit Disorder with Hyperactivity(ADHD), associated with a pattern of Bipolar Spectrum, its effective psychoterapeutic and psychopharmacological treatment.

**Methodology.**- A twelve-years-old adolescent, with a four year history of hypoprosexia, hyperactivity, inattention, and impulsivity in the context of family dysfunction. There was also occasional hyperphagia. He had received psychoterapeutical and psychopharmacological treatment to ODD, then to Attention Deficit Disorder with Hyperactivity and increased symptoms. We needed to change the psychopharmacological treatment, because still the sintomatology with irritability, distractibility, restlessness, anger outburst, hyperactivity, grandiosity and dysphoria. In the test of Young Mania Rating Scale and HCL-32, the results were compatible with BD. The new pharmacological treatment were with Antipsychotic. He had psychotherapeutic management-social skills- and family therapy. HAS (Haute Autorit+® De Sant+®). Now the prognosis is better(CHIPAE), and there is absence of irritability.

**Conclusions.**- The irritability dysfunctional, emotional dysregulation and impulse control deficits, have a high etiopathogenic relationship with Bipolar disorder in Adolescents, where the same psychotherapeutic treatment could be effective. However, the psychopharmacological treatment is a challenge and should be monitoring step by step

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Eur Psychiatry, 2018:48:S175.

FREE-T3 AS A BIOLOGICAL MARKER FOR A SUBGROUP OF CHILDREN WITH ADHD.

#### Caci H, et al.

**Introduction.**- Thyroid function of children with ADHD has been studied with an equivocal way. Some authors noticed similarities between ADHD symptoms and the Thyroid Hormone Resistance while others concluded that the thyroid function was normal based either on total-T3, free-T3, total-T4, free-T4 or TSH (Thyroid Stimulating Hormone). However, environmental factors may affect the thyroid function resulting in ADHD-like symptoms.

**Objectives**.- Our hypothesis was that a subgroup of children with ADHD would have higher levels of free-T3 (that is, the active hormone) and nevertheless has normal free-T4 and TSH levels.

**Methods**.- Retrospective analyses of systematic biological assays performed before prescribing any psychostimulant treatment to a child formally diagnosed with ADHD in our department since 2001.

Results.- No hypothyroid or hyperthyroid case in our sample of 498 children (including 90 girls). No effect of age and sex on free-T3, free-T4 and log(TSH) whatever the technique used (IECL/Centaur, EIA/Beckman, CMIA/Architect et ECLIA/Roche). 128 children (25.7%) had free-T3 levels beyond the reference interval provided by the laboratories on result sheets. Considering the two most frequent techniques, binomial law showed that 62 children out of 401 (15.5%) had free-T3 levels beyond the percentile 97.5 calculated on very large samples of children. Among them, the odds-ratio for a comorbid Oppositional Defiant Disorder (ODD) was 2.01 (P < .05).

**Conclusions.**- Analyses should be replicated in a multicentre, prospective and controlled study. The role of an isolated high free- T3 in ODD should be investigated. Finally, environmental factors should be investigated to understand the underlying mechanisms

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Eur Psychiatry. 2018;48:S378-S379.

DEFICIT OF MEMORY IN DELAYED RECALL CONDITION IN PRESCHOOL CHILDREN WITH ADHD.

#### Kiselev S.

**Background.**- It was shown that children with ADHD have deficit in prefrontal cortex function including deficit in working memory (Martinussen et al., 2012). In our previous research we have revealed that ADHD children at the age 8-9-years have deficit in memory in delayed recall condition (Kiselev et al., 2017). The goal of this research was to examine the hypothesis that preschool children with ADHD have the same deficit in memory in delayed recall condition as children at the age 8-9-years.

**Method and participants.**- The experimental group included 13 children with ADHD at the age 5-6-years. The control group included 13 typically developing children. The children from experimental and control group were matched for IQ, gender and age. Children from both groups were assessed with visual memory subtest from Luria's neuropsychological assessment battery. This subtest is designed to assess the ability to perform visual memory for objects in immediate and delayed conditions. Two-way ANOVA was used to reveal group differences in reproducing the objects in two conditions.

**Results.**-Wehave not revealed significant differences between children from experimental and control group in the reproducing the objects in immediate condition. However, the interaction of condition type and group was significant (p 0,05). ADHD children were less successful in reproducing the objects in delayed condition. In view of the obtained results, it can be assumed that preschool children with ADHD have specific deficit in memory in delayed recall condition

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Eur Psychiatry. 2018;48:S510.

PSYCHOTHERAPEUTIC INTERVENTIONS FOR ADHD IN PEOPLE WITH INTELLECTUAL DISABILITIES.

## Elstner S.

**Introduction.**- ADHD is a neurodevelopmental disorder can be which is typically diagnosed in child-and adolescent psychiatry and which can be often combined with behavioural problems. Also in people with intellectual disabilities (ID) challenging behaviour can also often be found with some comorbidity of ADHD. State of the art in treatment is a combination of pharmacological and psychotherapeutic strategies.

**Objectives**.- The study wants to give a comprehensive overview about the so far existing psychoptherapeutic strategies in ADHD in people with IDD.

**Methods**.- The database Pub Med was screened for psychotherapeutic strategies in ADHD by the keywords: Psychotherapy and ADHD (search history 1) and the combination search history 1 and £intellectual and disability or disabilities.

**Results.**- The output of search history 1 was much higher than the output of psychotherapy in ADHD for people with ID.

**Discussion**.- Although the psychotherapeutic strategies in ADHD seem to be elaborated with manuals, the group of people with ID is still neglected. There are some interesting programs for the treatment of impulsiveness and ID, which represents the beginning of treatment possibilities also for ADHD symptoms in people with ID

Eur Psychiatry. 2018;48:S248.

EFFECT OF BODY-ORIENTED THERAPY ON EXECUTIVE ABILITIES IN PRESCHOOL CHILDREN WITH ADHD.

## Kiselev S, Parshakova A.

**Background.**- It is known that children with ADHD have deficit in executive abilities. The gaol of this study was to reveal the effect of body-oriented therapy on executive abilities in preschool children with ADHD. We compared the efficacy of two methods of treatment (body-oriented therapy for children vs. conventional motor exercises) in a randomized controlled pilot study.

**Methods and participants.**- 12 children with ADHD between 5 to 6 years of age were included and randomly assigned to treatment conditions according to a 2+ù2 cross-over design. The body-oriented therapy included yogas' exercises and breathing techniques. To assess the executive functions and attention in children we used 5 subtests from NEPSY (Tower, Auditory Attention and Response Set, Visual Attention, Statue, Design Fluency). Effects of treatment were analyzed by means of an ANOVA for repeated measurements.

**Results.**- The ANOVA has revealed (P < .05) that for all 5 subtests on executive functions and attention the body-oriented therapy was superior to the conventional motor training, with effect sizes in the medium-to-high range (0.51-0.87).

**Conclusions.**- The findings from this pilot study suggest that bodyoriented therapy can effectively influence the executive abilities in preschool children with ADHD. However, it is necessary to further research the impact of body-oriented therapies on the prevention and treatment of ADHD in children

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Eur Psychiatry. 2018;48:S396.

CAN WE PREVENT SUBSTANCE USE DISORDER IN ADHD PATIENTS?

#### Saiz GH. et al.

**Introduction.**- The prevalence of is about 5% in children and 2.5%. This disorder is sometimes infradiagnosed because of its multidimensional symptoms, which can confuse the practioner to identify the core symptoms of ADHD. Validated assessment scales and high-yield clinical questions can help diagnose adults with ADHD. Patients with ADHD may be at high risk of developing a substance use disorder. It depends of many factors, such as impulsive behaviour, psychosocial problems, affective disorders or self-treatment of ADHD disorder with psycho-stimulant drugs.

**Methodology**.- A review was conducted aiming to clarify the triggers and possible mechanism of prevention in ADHD patients to prevent a EVoccurring substance use disorder. The literature search was conducted in Pub Med data reviewing articles dating between 2013 and 2017.

**Results.**- 1. Guidelines suggest that the most impairing symptom of ADHD should be treated first. But, for example, treating ADHD with SSRIs is related with an increase in substance-related events in short term. 2. Many studies have suggested that treating both adult and adolescents with stimulants for ADHD is related with a reduction of substance use disorder.3. Treatment of ADHD has also been associated with a reduction of psychosocial problems that can lead to substance use disorders.

**Conclusions.**- Early detection and treatment of ADHD is an important fact to prevent the future development of a substance use disorder. Untreated ADHD can lead to behavioural, social, functional and mental health problems. Some studies may suggest a need for increased doses in population with SUD to achieve optimal ADHD symptom control

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Eur Psychiatry. 2018;48:S371-S372.

WHICH SIDE DOES THE MASS MEDIA TAKE ON THE DEBATE ON ADHD?

Alvarez De Mon GM, Pereira V, Dot T, et al.

**Introduction.**- Information on health and disease is one of the priority interests of people in countries with high economic development. Increasingly, patients and their families seek information about it on the internet and on social networks.

**Objective.**- To conduct a qualitative analysisonthe Tweets that refer to ADHD from the Twitter accounts of prominent US mass media outlets.

**Methods.**- Fifteen US news media outlets were selected and analysed. These outlets were chosen based on the number of followers on their Twitter accounts and were narrowed down to those with the most followers. The Tweets were selected if they made any reference to ADHD (ex. ADHD from @nytimes). This study focused on the Tweets from 2007-2016.

**Results.**- Overall, 208 Tweets were selected and divided into four categories. 50 focused on general interest (Common symptoms of women with ADHD), 92 were testimonies from patients (Simone Biles proudly opens up about having ADHD), 38 revolved around scientific advancements (Research shows Omega-3 fatty acids helped improve attention spans of boys with or without ADHD) and 28 had a condescending tone towards these disorders

**Conclusions.**- The rise in ADHD diagnosis has been one of the most controversial issues in psychiatry in the past ten years. Twitter perfectly reflects this truth by presenting both sides of the argument. On one hand, users turn to Twitter to reinforce the existence of ADHD by giving personal testimonies and statements. Conversely, doubters use Twitter to not only express their disbelief in the disorder, but also attack both doctors and patients

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Eur Psychiatry. 2018;48:S248.

MULTIPLE COMORBIDITIES IN A FIDGETY CHILD: SOTOS SYNDROME TYPE I WITH ADHD, HYPOTHYROIDISM, ANEMIA, VITAMIN D DEFICIENCY, ABNORMAL EEG AND BORDERLINE INTELLIGENCE QUOTIENT.

Mohinder Singh DK, Jha P, Ghildiyal V, et al .

**Introduction.**- There is sparse data on Sotos syndrome in the contextual interplay of neuropsychiatric and medical comorbidities.

Objectives.- To report a rare case report of multiple comorbidities in a 7-year-old fidgety boy.

Methods.- Case report. Master Y, a 7-year-old boy presented to the child psychiatry clinic brought by his parents with chief complaints of problems in his studies, hyperactivity, inattentiveness, behavioral problems since past few years. No features of autism were reported. Mild Facial dysmorphism was noted in physical examination. The child was not cooperative for formal mental status examination and was very restless, inattentive, hyperactive and fidgety.

Results.- Patient was diagnosed with ADHD (combined type). His blood report revealed iron deficiency anaemia (Hemoglobin 9 g) and severe vitamin D deficiency and an elevated TSH (8.61). His EEG profile revealed sharp waves over frontal region and generalized epileptiform activity. He was started on Thyroid Hormone, VitaminDand Iron Supplements from Pediatrics. He was diagnosed with Sotos Syndrome type I from Pediatric Neurology after clinical evaluation and appropriate genetic testing and was given clearance for Methyl Phenidate for ADHD and no antiepileptics were advised. IQ testing according to WISC testing came to 82. Tablet Methyl Phenidate 10mg od and behavior therapy and OT was advised. His subsequent EEG and blood tests were normal and is doing clinically well.

**Conclusions.**- Sotos sydrome Type I can have ADHD and interplay of thyroid dysfunction, iron deficiency anemia, EEG abnormalities and Vitamin D deficiency as seen in our case

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Eur Psychiatry. 2018;48:S501.

ADULT ATTENTION DEFICIT HYPERACTIVITY DISORDER: THE EVMORBIDITY OF PERSONALITY DISORDERS THAT SUGGEST THE NEED FOR MORE HOLISTIC INTERVENTIONS.

Jain U, Jain S.

Previous literature shows the strength of the assortment thatADHD of the Combined Subtype EVsegregate with Cluster B Personality Disorders (PD) and ADHD of the Inattentive Subtype EVsegregate with Cluster C PD. There is very little work being done on other strategies to address the impairment related to chronic PD factors which do not disappear with drugs. However, it may facilitate some of the other interventions beginning with the motherhood of all interventions: sleep, nutrition and exercise. In this paper, evidence-based interventions are discussed related to the former but exercise, as yet in pilot form, are presented.

**Method**: Ten Olympians, with childhood ADHD, were interviewed. Components of their exercise were reviewed to determine if there was a commonality to the protective factor that exercise embraced. The assessments were an open dialogue with probing questions. However, the same questions were given to each participant.

**Results.**- The factors that were consistently represented in all ten individuals that were relevant were a) mentorship/coaching b) structure of the training regimen c) early exposure before the age of 11 and d) embracing a discipline around nutrition and sleep.

**Conclusions.**- There were many other factors presented but this early discussion begins to point to resiliency strategies we should be employing within children early in their lives. All of the participants said they were on medications after they were diagnosed but did not need medications subsequent to their entry into competitive sports. This data needs to be replicated and widened to seek out factors of importance

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Eur Psychiatry. 2018;48:S141.

DISRUPTIVE MOOD DYSREGULATION DISORDER IN OFFSPRING OF PARENTS WITH ADHD.

## Abouzed M, Elawady A.

**Background**.-Emotion dysregulation, is common in ADHD and may arise from deficits in orienting toward and processing emotional stimuli It, Disruptive mood dysregulation(DMDD) in the offspring of parents with ADHD under estimated and this but the specificity of this association has not been established.

**Aims**.- We examined the specificity of DMDD to family history by comparing offspring of parents with ADHD WITH a control group without psychiatric disorders.

**Method**.- 112 children who are offspring of parents with ADHD and 100 children for normal parents without ant psychiatric disorders and age and sex matched. We diagnose DMDD using the Schedule for Affective Disorders and Schizophrenia for School Aged Children for DSM-5 in 180 youth aged 6-18 years (KSADS-PI).

**Results.**- Diagnostic criteria for DMDD were met in 21 (18.75%) of the offspring of parents with bipolar disorder, 6 (6%) of the control offspring. With P-value < 0.001.

**Conclusions.**- Our results suggest that Disruptive mood dysregulation (DMDD) is may be associated with a family history of ADHD

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Eur Psychiatry. 2018;48:S329-S330.

MINDFULNESS-BASED COGNITIVE-BEHAVIORAL THERAPIES FOR TREATMENT OF ATTENTION DEFICIT HYPERACTIVITY DISORDER IN CHILDREN AND ADOLESCENTS: A LITERATURE REVIEW.

#### Khan T, Cosme R.

**Introduction.**- Attention-deficit/hyperactivity disorder (ADHD) is a common psychiatric disease in children. Despite the demonstrated effectiveness of current ADHD medications, treatment discontinuation is fairly common. In recent years, there has been evidence that mindfulness meditation strengthens attention regulation [1-3] and improves some executive functions [4]. This approach offers a novel and potentially useful tool in the multimodal treatment of ADHD.

**Objective.**- Our objective is to evaluate and review the current literature on the effectiveness of implementation of mindfulness techniques in children and adolescents suffering from ADHD.

**Methods.**- We examined a total of 7 studies [5-11], 3 interventional studies and 4 literature reviews. Interventional studies, as described in detail in Table 1, use mindfulness techniques with treatment and control groups. 4 literature reviews are described in detail in table 2.

**Results.**- All interventional studies favor the beneficial effects of mindfulness techniques in improving symptoms of ADHD. Out of the 4 literature review studies, 1 provides support for the feasibility of mindfulness-based interventions, 1 remains inconclusive due to high risk of bias and 2 provide evidence of benefit in both adults and children suffering from ADHD.

**Conclusion.**- Thus we conclude that there is strong evidence to support that mindfulness-based therapies have a beneficial effect on improving attention, behavior and in some cases lifestyle of the patients suffering

from ADHD and their parents. However, there is much need for further evidence-based research in this area, in order to establish this treatment modality as standard of care for children and adults with ADHD

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Eur Psychiatry. 2018;48:S300.

BIPOLAR DISORDER IN ADHD: FREQUENT COMORBIDITY OR SEVERE NEURODEVELOPMENTAL DISORDER? Oliva F, Ferreri P, Portigliatti PA, et al.

**Background.**- The aim of the present study was to evaluate prevalence and clinical variables of patients with and without bipolar disorder in a sample of adult ADHD outpatients.

**Methods.**- We examined all medical records of outpatients accessing the adultADHDcenter of theAOUSan Luigi Gonzaga, Orbassano (TO), Italy, in order to collect data about socio-demographic factors, medical history, medical and psychiatric diagnosis. Adult DSM-IV ADHD diagnosis was made by DIVA 2.0 whereas DSM-IV comorbidities were assessed by SCID I and II.

**Results.**- Above one quarter of our sample with ADHD (26,6%) had also a bipolar disorder that was a type II in almost all of cases (90,5%). ADHD combined type (ADHD-C) is more common than inattentive type (ADHD-I) in patients with bipolar disorder only (ADHD+DB; ADHD-C:85,7% vs. ADHD-I:14.3%; ADHD; ADHDC: 51,7% vs. ADHD-I:48,3%; p=0,006). ADHD-C is more common in bipolar patients even in childhood (ADHD+DB; ADHD-C:65% vs. ADHD-I:25% vs. ADHD-H:10%; ADHD; ADHD-C:52% vs. ADHDI: 48%; P = 0.048). Moreover, ADHD with bipolar disorder had more frequently a comorbid psychiatric disorder or other co-occurring conditions (personality disorder, 19% vs. 1,8%, P = 0.006; sleep disorder, 52.3% vs. 32.7%, P = 0.009; use of benzodiazepines without anxiety disorder, 47.6% vs. 10.9%, P = 0.001; immune system disease, 23.8% vs. 5.2%, P = 0.015).

**Conclusions.**- Our findings are consistent with previous studies reporting a high prevalence of bipolar II disorder among adults with ADHD. ADHD patients with comorbid bipolar disorder seem most likely to have shown a combined manifestation of inattention and hyperactivity in childhood that evolved in a complex and severe clinical picture with personality and sleep disorders co-morbidities

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Eur Psychiatry. 2018;48:S384.

EFFECTIVENESS OF TREATMENT FOR CHILDREN WITH ADHD AND AUTISM WITH NOOFEN.

## Shahini M, Ahmeti A.

Attention Deficit Hyperactivity Disorder (ADHD), especially when it is in comorbidity with autism, is a challenge in psychiatric treatment. Noofen has been found to have demonstrated a positive effect onADHDchildren by improving cognitive, self-control, focus, attention distribution, and verbal memory. The purpose of this study was to assess the effectiveness of Noofen in the treatment of Hyperactivity and Autism in children ages 4-11. Participants were children who have sought medical help at the Mental Health Center for Children and Adolescents. In this pilot study are included 12 children, and it was done during 2016, over a period of three months. 10 of the participants were male and two females. The average age of the participants was M= 7.08 (SD = 2.46). Children have been diagnosed with childhood psychiatric hyperactivity disorder and are treated with NOOFEN with an average dose of 250mg to 500 mg. The NOOFEN Dosage was made according to a psychiatric preparedness scheme. The results showed that 11 children had improved symptoms of hyperactivity, while one of the children reported improvement, but was discontinued due to the anaesthesial effect (headache). Participants were also monitored through CBCL in improving the symptoms of hyperactivity as well as through direct interviews with parents. This pilot study has shown that treating the symptoms of hyperactivity with attention deficit as well as some of the symptoms of autism is effective in the short term, especially in attention and language but we do not currently have the effects for a longer time

Eur Psychiatry. 2018;48:S249.

NON-SYNDROMIC OROFACIAL CLEFTS AND INCREASED RISK FOR PSYCHIATRIC DISORDERS.

Tillman K, Hakelius M, Ramklint M, et al.

**Introduction.**- Being born with an orofacial cleft (OFC) can increase the risk of poor academic achievements and psychological health later in life.

**Objectives**.- To investigate the risk of psychiatric diagnoses in individuals with OFC, stratified by cleft type, compared with individuals without OFC and healthy siblings.

**Methods.**- A nationwide register-based cohort of all individuals born in Sweden with OFC between 1973 and 2013 (n = 7842) was compared to a comparison cohort of healthy individuals (n = 78,409) as well as to their healthy siblings. By linking to Swedish registers, we examined the risk of psychiatric diagnoses, suicide attempts and suicides by using Cox regression. The analyses were adjusted for perinatal factors, genetic syndromes and associated anomalies, parental socioeconomic factors as well as parental psychiatric morbidity and history of suicide attempts.

**Results.**- Children with non-syndromic OFC had a significantly higher risk of intellectual disability, language disorders, ADHD, ASD, psychosis and behavioral and emotional disorders with onset in childhood, compared with individuals without OFC. Children with cleft palate only (CPO) had the highest risks and those with cleft lip (CL) the lowest. No increased risks were found regarding suicide or suicidal attempts. The healthy siblings of patients with OFC were less likely to be diagnosed with a psychiatric disorder.

**Conclusions.**- Children with non-syndromic OFC have increased risk for several neurodevelopmental disorders. The sibling analyses suggest that the higher risk cannot

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Eur Psychiatry. 2018;48:S8-S9. EPIDEMIOLOGY OF ADHD AND SUD. Clerici M, Di GE, Colmegna F.

Attention-deficit/hyperactivity disorder (ADHD) has been primarily considered, for a long time, a childhood condition. Despite it, recent data suggest that symptoms of ADHD continue into adulthood in up to 50% of people diagnosed as affected by ADHD during their childhood. Accurate diagnosis of ADHD in adults is challenging and requires attention to early development and symptoms of inattention, distractibility, impulsivity and emotional liability. Currently, it does not exist a gold standard for its diagnosis, and we demonstrated a low reliability of screening test such as the Brown ADD Scales in populations at risk (e.g. acute psychiatric inpatients and parents of children affected by ADHD). Moreover, diagnosis is further complicated by the overlap between the symptoms of adult ADHD and the symptoms of other common psychiatric conditions such as depression and substance abuse. While stimulants are a common treatment for adult patients with ADHD, they are often used as a self-treatment, especially in patients who lack of a correct diagnosis and treatment. Antidepressants may also be effect tive, while cognitive-behavioural skills training and psychotherapy are useful ifadjuncts to pharmacotherapy. Addiction thus embodies a key point in differential diagnosis as well as it might be considered an adverse effect of a long duration of untreated illness. As a consequence, it should be accurately checked and weighted during the diagnostic process

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Eur Psychiatry. 2018;48:S178-S179.

EFFICACY OF A THIRD WAVE COGNITIVE BEHAVIORAL THERAPY FOR ATTENTION DEFICIT HYPERACTIVITY DISORDER. Villadoro C, Lopez CJ, Crouzet L, et al.

**Introduction.**- Attention Deficit Hyperactivity Disorder(ADHD)represents most of the consultations in Childhood Psychiatry settings. Medical treatment is helpful for severe cases, but more effective psychosocial therapies are needed.

**Aims**.- We examined the efficacy of amindfulness-based cognitive behavioral therapy (mCBT) for children diagnosed with ADHD and their parents, compared to those receiving usual treatment.

**Method**.- An open trial with two parallel arms was conducted at the child psychiatry department of Nimes University Hospital from October 2016 to June 2017. ADHD children were allocated to the intervention group

or treatment as usual. mCBT consisted on 16 weekly sessions which were conducted separately for children and their parents. Children in the waiting list received no specific intervention. Changes in ADHD rating scale scores from inclusion to the last visit (3 months later) were the primary outcome. Secondary outcomes included anxiety and depression scales.

**Results.**- ADHD symptoms decreased in the group following the mCBT compared to the waiting list (average score decreases: 5.9-\;\frac{1}{7.1} vs. 2.6-\;\frac{9.7}{9.7}, respectively). Sex ratios (73% males in both groups) and time lapses between assessments (average time in months: 4 and 3.4, respectively) were similar in both groups, but patients in the waiting lists were slightly younger and received psychopharmacological treatment less often. **Conclusion.**- We will present the preliminary but promising results of an innovative third-wave CBT for ADHD children. Compared to classical parental guidance intervention, this therapy is enhanced with mindfulness techniques and simultaneously followed by the children and their parents

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Homeopathy. 2016;105:28-29.

RATIONALE FOR A PRAGMATIC RANDOMISED CONTROLLED TRIAL OF THE EFFECTIVENESS OF TREATMENT BY HOMEOPATHS FOR ADHD.

#### Fibert P.

**Objective**: To design a trial with minimal potential for bias (maximal internal validity) representing treatment by homeopaths as experienced in routine clinical practice (maximal external validity) informing ADHD stakeholders such as families and decision makers in health, education, social work and criminality.

**Methods**: Recruitment of a long term observational cohort of children with ADHD. Measurement of subjective outcomes (parent measurement of core ADHD symptoms, anger and wellbeing); blinded outcomes (teacher rated core ADHD symptoms, classroom disruption); and objective outcomes (criminality, school exclusion, attendance, and costs). A random selection of cohort participants meeting trial criteria is offered treatment by homeopaths or essential fatty acids. Those meeting trial criteria not randomly selected act as a 'treatment as usual' control group. Primary analysis compares the clinical and cost effectiveness of each intervention with treatment as usual.

**Results**: Internal validity. Comparing more than one intervention ensures that biases associated with unblinded studies (e.g Hawthorne effects) are equally distributed across groups. Unblinded parent reported outcomes are at risk of expectation biases. Measurement of blinded outcomes by teachers, and objective outcomes such as levels of criminality, resource use, school exclusion and attendance, minimises the risk of biased outcome assessment. External validity. The design assesses the real world effectiveness of the total package of care (provision of individualised homeopathic remedies, freedom to change remedies and potency, and regular consultations). It assesses the therapeutic potential of the intervention; it measures objective outcomes of interest and cost effectiveness which provides useful information for stakeholders; and it addresses treatment bias towards interventions suitable for blinded studies.

**Conclusion**: Previous trials have assessed the efficacy of homeopathic remedies and probably underestimate effects due to the interacting nature of components. Complex therapies such as homeopathy are best measured in their totality but potential for bias must be addressed

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Homeopathy. 2018;107.

PRELIMINARY FEASIBILITY AND CLINICAL RESULTS OF A PILOT STUDY OF TREATMENT BY HOMEOPATHS FOR CHILDREN WITH ADHD USING THE TRIALS WITHIN COHORTS (TWICS) DESIGN.

#### Fibert P, Relton C.

**Background**: There is a need to improve outcomes for attention-deficit hyperactivity disorder (ADHD) which is a strain on stakeholder services and at risk of negative outcomes. Information is required about treatments that can achieve improvements in emotional regulation, criminality, school disruption, and ADHD in autism. Trials of individualised homeopathic remedies for ADHD show positive results. Trials of treatment of children with ADHD by a homeopath as experienced in clinical practice can provide useful information about the potential of homeopathic treatment to improve outcomes.

**Methods**: This study used the Trials within Cohorts (TwiCs) design. Participants were recruited to a long-term observational ADHD cohort and their outcomes of interest (ADHD symptoms, quality of life, school disruption, resource use and criminality) measured every 6 months. A random selection was offered treatment by a homeopath (arm 1) or a nutritional therapist (arm 2), while the remainder acted as a virtual treatment as usual (TAU) control arm (arm 3). The effectiveness of the interventions, feasibility of recruiting to the cohort, delivering the interventions, and measuring outcomes were assessed.

**Results**: Assessment of 6-month outcomes will be conducted in March 2017. One hundred and fifty participants were recruited to the cohort between September 2015 and 2016, of whom 124 were eligible for the pilot study. Measurement of outcomes was feasible, although non-return of measures was a feature. Delivery of the interventions face to face and online was feasible and provided flexibility for this population. **Conclusion**: This pragmatic trial design allows the testing of treatment by homeopaths as experienced in usual practice over the long term. It provides important information to stakeholders about the potential effects of homeopathic treatment. Attrition and non-attendance were features. They are common in ADHD trials, and providing evidence about the acceptability of interventions is therefore useful

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Hum Brain Mapp. 2018;39:3449-67.

NOVEL IN SILICO MULTIVARIATE MAPPING OF INTRINSIC AND ANTICORRELATED CONNECTIVITY TO NEUROCOGNITIVE FUNCTIONAL MAPS SUPPORTS THE MATURATIONAL HYPOTHESIS OF ADHD.

#### de LN. Kodish I. Rachakonda S. et al.

From childhood to adolescence, strengthened coupling in frontal, striatal and parieto-temporal regions associated with cognitive control, and increased anticorrelation between task-positive and task-negative circuits, subserve the reshaping of behavior. ADHD is a common condition peaking in adolescence and regressing in adulthood, with a wide variety of cognitive control deficits. Alternate hypotheses of ADHD emphasize lagging circuitry refinement versus categorical differences in network function. However, quantifying the individual circuit contributions to behavioral findings, and relative roles of maturational versus categorical effects, is challenging in vivo or in meta-analyses using task-based paradigms within the same pipeline, given the multiplicity of neurobehavioral functions implicated. To address this, we analyzed 46 positively-correlated and anticorrelated circuits in a multivariate model in resting-state data from 504 ageand gender-matched youth, and created a novel in silico method to map individual quantified effects to reverse inference maps of 8 neurocognitive functions consistently implicated in ADHD, as well as dopamine and hyperactivity. We identified only age- and gender-related effects in intrinsic connectivity, and found that maturational refinement of circuits in youth with ADHD occupied 3-10x more brain locations than in typical development, with the footprint, effect size and contribution of individual circuits varying substantially. Our analysis supports the maturational hypothesis of ADHD, suggesting lagging connectivity reorganization within specific subnetworks of fronto-parietal control, ventral attention, cingulo-opercular, temporo-limbic and cerebellar sub-networks contribute across neurocognitive findings present in this complex condition. We present the first analysis of anti-correlated connectivity in ADHD and suggest new directions for exploring residual and non-responsive symptoms

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Int J Psychophysiol. 2016;108:59.

OSCILLATORY DYNAMICS OF THE ODDBALL RESPONSE IN CHILDREN WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER.

## Karakas S, Dogutepe E, Erdogan B.

Oddball paradigm triggers the P300 component. The component is predominantly formed by the delta oscillation and is responsible from attention and working memory (context updating), to which attentional processing is closely linked. Attention deficit hyperactivity disorder (ADHD) is customarily approached using pharmacotherapy while other techniques such as biofeedback uses training involving oscillatory components. The present study compares the oscillatory activity in the oddball response of the ADHD and control groups under an experimentally produced attentional state. The sample included 6-12-year-old boys

with ADHD (combined subtype: 49 cases, attention deficit subtype= 17 cases), and age-matched healthy controls (n= 40). Children were first referrals and were not on pharmacotherapy. Exclusion criteria were neurological and/or psychiatric comorbidity other than ADHD and intelligence level outside the 85-129 IQ range. In the auditory oddball paradigm, the 25 % deviants were 1000 Hz and the 75% standards were 2500 Hz (ISI= 1500 msec). Particiants were asked to count the deviants and report them at the end of the recording session. Attention was maintained using the stimulus omission paradigm. The paradigm included a series of equally-spaced (ISI= 1500 msec) visual stimuli (circles) every fourth of which was omitted. The participants were asked to attend to the consecutive stimuli and indicate the time point at which the 5th stimulus should occur by a button-press response. The oddball and stimulus omission paradigms were given in alternating order. The difference between the response accuracy rate of the control and clinical groups were not significant. The delta component was extracted in the time-plane and time-frequency planes. Digitally filtered delta and theta oscillations were not significantly different in amplitude and latency between the clinical and control groups. In the time-frequency plane, the configuration of responses to the standard stimuli were not significantly different between the groups. The deviant response of the control group was characterized by a frontally recorded theta component followed by two delta components. Otherwise, time-frequency layout of the oscillatory components were similar between the groups. In ADHD, P300 latency is longer and amplitude generally higher. When cases were kept at an enduring attentional state, delta and theta oscillatory responses that contribute to the morphology of P300 became similar. These results show that the ADHD symptoms may temporarily subside upon appropriate cognitive manipulations. The stability and ecological validity of this improvement, however, needs to be studied in future reserach

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Int J Psychophysiol. 2016;108:143-44.

## DEFICIT IN MEMORY FOR WORDS IN DELAYED RECALL CONDITION IN ADHD CHILDREN.

#### Kiselev S, Lvova O.

It is known that children with ADHD have deficit in different cognitive abilities (Kipp, 2005 et al.). Particularly, children with this disorder have working memory deficit (Martinussen et al., 2012). In our previous researches we have shown that ADHD children have deficit in memory for faces and for names in delayed recall condition (Kiselev & Lvova, 2014; Kiselev & Lvova, 2016). In addition, we have found that ADHD children have weakness in reproducing the Rey-Osterrieth Complex Figure in delayed recall condition (Kiselev, 2015). The goal of this research was to examine the hypothesis that children with ADHD have weakness in memory for words in delayed recall condition. The experimental group included 18 Russianspeaking children with ADHD at age 7-8-years (13 boys and 5 girls). The control group included 18 typically developing children. The children from experimental and control group were matched for IQ, gender and age. Children from both groups were assessed with Luria's child neuropsychological battery using Memory for words subtest. This subtest is designed to assess the ability to learn and recall six words in immediate and delayed recall conditions. Each child was asked to recall six words immediately after first presentation and 30-min later. Two-way ANOVA with repeated measures was used to reveal group differences in reproducing the words in immediate and delayed recall conditions. We have not revealed significant differences (pΓëñ0,05) between children from experimental and control group in recalling the words in immediate condition. However, the interaction of condition type and group was significant (pΓëñ0.05). ADHD children were less successful in recalling the words in delayed recall condition. This research has shown that ADHD children have deficit in memory for words in delayed recall condition. In view of results that were obtained in our previous researches it can be assumed that children with ADHD have specific memory deficit the weakness in recall in delayed condition

Int J Psychophysiol. 2016;108:128.

EFFECTS OF ACUTE EXERCISE ON RESTING EEG IN CHILDREN WITH ATTENTION-DEFICIT HYPERACTIVITY DISORDER. Hung T-M, Huang C-W, Huang C-J, et al.

Children with attention deficit hyperactivity disorder (ADHD) are characterized by a deviant pattern of brain oscillations during resting state compared to normal children, particularly elevated theta power and decreased alpha and beta power. Increased theta/alpha and theta/ beta ratios have been related to cognitive functioning and acute exercise has been found beneficial to cognitive function. Therefore, it was worthy to explore the effect of acute exercise on resting-state electroencephalograph (rEEG). The first part of the present studywas to investigate the rEEG differences between ADHD and typically developed (TD) children. The second part was to examine the effect of acute exercise on the rEEG in children with ADHD. rEEG was recorded during eyes-open resting for 23 TD and 19 children with ADHD combined subtype (all boys). Results indicated that ADHD children exhibited lower alpha power in central and central parietal region compared with TD. In addition, smaller theta in frontal, central, central parietal was observed subsequent to acute exercise in comparison to video control. These findings supported deviated rEEG between normal and ADHD children and rEEG could be changed after acute exercise

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Int J Psychophysiol. 2016;108:74.

FUNCTIONAL CONNECTIVITY AND ELECTROENCEPHALOGRAPHIC DIFFERENCES IN TWO SUBTYPES OF ADHD.

### Carricarte TJ, Romero Y, Reigosa V.

Attention Deficit Hyperactive Disorder (ADHD) is the most common neurodevelopmental disorder. Diagnosis are subjectively guided by clinical criteria based on the frequency of occurrence of the symptoms and how they interfere in the patient's life. Up to date, many researches have tried to find suitable ADHD biomarkers in order to gain precision in the diagnosis. A noticeable number of candidates stem from electrophysiological measures mainly obtained by electroencephalographic (EEG) recordings. However, quantitative EEG findings in ADHD patients and healthy subjects haven't been neither conclusive nor consistent. In this study, we employed a conventional quantitative method and a new EEG approach based on functional connectivity, a method scarcely used in previous ADHD studies. EEG data were obtained during eyes closed resting-state from 12 and 6 children diagnosed as ADHD combined subtype and inattentive subtype, respectively. The statistical dependency between each pair of electrodes for each frequency band (delta, theta, alpha and beta) was generated calculating the synchronization likelihood. The resulting connectivity matrixes were converted into weighted graphs and characterized by global and local network properties: the clustering coefficient, characteristic path length and global and local efficiency. In addition, the absolute and relative powerswere calculated for each frequency band. Overall, the synchronization networks were different between ADHD subtypes. Global efficiency was higher in the inattentive subtype compared to the combined subtype for the alpha and delta frequency band. When compared with age-standardized EEG norms, there were no statistical differences in the absolute and relative powers in the ADHD group (inattentive and combined). However, differences in these measures were found between ADHD subtypes. These results support the hypothesis of a significant heterogeneity across ADHD subtypes, suggesting either a different underlying neural mechanism or differences in the functioning of the same neural mechanism. The findings are explained on the light of differences in functioning of the dopaminergic mesolimbic branch between subtypes

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Int J Psychophysiol. 2016;108:121.

REPETITIVE-TRANSCRANIAL MAGNETIC STIMULATION IN CHILDREN WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER: EFFECTS ON BEHAVIOR AND P300 EVENT-RELATED POTENTIAL.

Baez-Martin MM, Gomez-Fernandez L, Vidal-Martinez B, et al.

**Background**: Attention deficit hyperactivity disorder (ADHD) is common in childhood and includes inattention, hyperactivity and impulsivity that influence learning and social behavior. Event-related potentials (ERPs) provide information about the temporal course of cognitive processes in the brain. There are

evidences about the use of these responses, especially of P300 component, to evaluate cognitive changes in children with ADHD after various therapeutic strategies. On the other hand, repetitive Transcranial Magnetic Stimulation (rTMS) over dorsolateral prefrontal cortex (DLPfC) can induce an increase of dopamine release in the caudate nucleus.

**Aim**: to evaluate the probable effects of rTMS as a novel therapeutic tool in a group of children with ADHD by measuring the P300 ERP and its behavioral correlates.

**Subjects and methods**: Eight boys between 7 and 12 years old received a daily 40 minutes session of rTMS while they watched cartoons. This procedure was applied during five consecutive days. Patients were evaluated before treatment and after the last session. A visual odd-ball task with 20 % of randomized infrequent stimuli was presented while children pressed a bottom and performed a mental count of them. The records were obtained with a Medicid 3E equipment (Neuronic, SA) using the EP workstation and Neuronic Stimulator. Parents gave their signed consent to participate in the study.

Results: P300 component was maximal in parietal and occipital regions. There were no statistically significant differences in latency and amplitude of P300 component before and after treatment (Wilcoxon test, pN.05). However, the latency of P300 showed a negative correlation with the precision of the task (Spearman correlation's test pb.05). A significant reduction of the simple reaction time was observed in the recordings after treatment (Wilcoxon test, pb.05). Furthermore, four children showed a reduction in the number of incorrect responses or an absence of them after treatment, in agreement with the improvement of behavioral and academic results reported by teachers and parents in all cases, based on a better punctuation in the list of symptoms of DSM-IV.

**Conclusions**: rTMS may modulate the behavior of children with ADHD, despite it was not totally confirmed with ERP results

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Int J Psychophysiol. 2016;108:6.

WOMEN ARE DIFFERENT TO MEN: EEG DIFFERENCES IN DSM-5 ADULT ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.

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

Attention-Deficit/Hyperactivity Disorder (AD/HD) has been classically characterised by elevated behaviours of hyperactivity, inattention, and impulsivity. Although AD/HD was initially conceptualised as a predominantly male childhood condition, it is now widely known to persist into adulthood, with increasing recognition in females. For the first time, the DSM-5 has recognised AD/HD as a disorder that often persists into adulthood. This study explored EEG sex differences of adults diagnosed with AD/HD (with an initial childhood diagnosis) according to DSM-5 criteria. Eyes-closed resting EEGs were recorded from 16 females and 16 males with adult AD/HD, and sex-matched control groups. EEGs were Fast Fourier transformed and estimates for total power, absolute and relative power in the delta, theta, alpha, beta and gamma bands, and the theta/beta ratio, were analysed across nine cortical regions. A secondary group interaction analysis allowed reporting on the statistical significance of male and female differences rather than the differences between significance levels. Interestingly, no global effects emerged between females with and without AD/HD. In contrast, maleswith AD/HD, compared with male controls, had globally reduced absolute beta, globally elevated relative theta, and a larger theta/beta ratio, consistent with the male AD/HD-EEG literature. Additionally, significant group interactions indicated that globally elevated relative theta and elevated frontal-midline theta/beta ratio noted in males with AD/HD differed significantly from results in females. The lack of significant differences between adult females with and without AD/HD suggests that there is less EEG variance among adult females than adult males, with and without AD/HD, and is consistent with the notion that males with AD/HD have more anomalous EEG profiles than femaleswith AD/HD.Women are different tomen, but this is the first study to report on an exclusively female adult AD/HD subject group. We conclude that the EEG profiles in this disorder differ significantly between women and men, warranting further independent examinations of AD/HD in females

Int J Psychophysiol. 2016;108:137-38.

PSYCHOPHYSIOLOGICAL CORRELATES OF ATTENTION DEFICIT HYPERACTIVITY DISORDER IN CHILDREN.

## Savchuk LV, Polevaia SA, Fedotchev AI, et al.

Attention Deficit Hyperactivity Disorder (ADHD) is the most common cause of behavioral disorders, learning difficulties, school dysaptation. Currently, diagnosis is based on clinical criteria only. Research of psychophysiological correlates of ADHD in middle childhood (children 7-12 years of age) is very actual. In our work, instrumental methods for a quantitative assessment of functional hemispheric asymmetry (FHA) and emotiogenic changes of function of color discrimination are presented. To assess selective attention and activity level the Toulouse-Pieron test was applied. The measurement of FHA is based on the preceding effect of dichotic sound stimulation. We estimated level of the FHA by the values of the threshold interaural delays. The computer campimetry is the measurement of color discrimination thresholds in the framework of HLS color model. 41 subjects between 7 to 12 years of age participated in the study: 18 children with ADHD and 23 children without diagnosis. In 68% of children with ADHD the right brain hemisphere is dominant. During dichotic stimulation with increasing interaural delay there is decrease in lability and excitability parameters for both the right and the left hemisphere (p = 0,001, t-tests). Concerning the indicators of stability, the significant differences from healthy children are not revealed. In hyperactive children, the color discrimination thresholds in all shades are reliably higher than in healthy children. In 91% of healthy children the function of color discrimination with the maximum differential threshold in green shades range prevails. in 70% of children with ADHD-in blue shades range. The indicators of computer campimetry which are closely related to indicators of accuracy (r = -0.87; p < 0.05) and speed (r = -0.93; p < 0.05) according to the Toulouse-Pieron test are revealed. The ranges of parameters of color discrimination function and sound localization function specific for children with ADHD are determined. Deterioration of color discrimination in shades of blue and domination of the right hemisphere can be considered as possible markers of the increased risk of clinical ADHD development in children aged 7-12

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Int J Psychophysiol. 2016;108:132.

INDEPENDENT COMPONENTS OF EVENT RELATED POTENTIALS: DIFFERENCES BETWEEN CHILDREN AND ADULTS WITH ADHD.

#### Markovska-Simoska S, Pop-Jordanov N.

The stages of information flow are measured by event-related potentials (ERPs). Using the independent component analysis (ICA) method, ERPs can be decomposed into functionally different components. Attention deficit hyperactivity disorder (ADHD) is a disorder involving deficits in attention and behavioral control. The aim of this study was to investigate the difference in independent components of ERPs between children and adults with ADHD compared to normal control groups. 30 children and 30 adults with ADHD as well as control groups consisted of 20 normal children and 26 normal adults, matched by age and gender, were examined. All ADHD participants met the full criteria for ADHD according to DSMIV. The Visual Continuous Performance Test (VCPT) as modification of GO/NOGO paradigm was applied. Omission, commission errors, reaction time and variation of reaction time were assessed as behavioral parameters of test performance. Amplitude and latency of the cognitive event-related ICA components (P3supF-motor inhibition component, P3bP-engagement component, P4monCC-monitoring component, P4vmF-working memory component, vcomTL and vcomTR-comparison components) from Fz, Cz, Pz, T5 and T6 were measured and analyzed in each test subject. Behavioral parameters showed significantly increased number of omission and commission errors and longer reaction time in ADHD children compared to normal corresponding control group. Variation of reaction time was significantly larger in both ADHD groups (children and adults) compared to control groups. Lower P3supF amplitude at the Cz electrode was obtained in children with ADHD compared to normal children (pb0.01). A significant lower amplitude of P4monCC and P4wmF components at Cz electrode, was found in children with ADHD compared to corresponding control group (pb0.01). Only adults with ADHD showed a significantly longer latency and lower amplitude of P3bP at Pz electrode compared to normal control adults (pb0.01). No differences in other ERP indices were found between children and adults with ADHD and controls. sLORETA was applied for source localization for each ICA ERP component. The ICA-ERPs components (P3supF, P4monCC and P4wmF) were significantly affected in children with ADHD, compared to normal controls, while P3bP was significantly changed only in

ADHD adults. These results are in favor with the typical clinical picture of ADHD with more pronounced hyperactivity problems (due to reduced motor inhibition component) in children that decreases with age and prevailing inattention problems in adults (lower action initiation component). Thus, Go/NoGo test and ICA-based method of analysis might provide a new approach for additional objective diagnostics of ADHD

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Int J Psychophysiol. 2016;108:28.

COGNITIVE NEUROSCIENCE APPROACHES TO ADHD.

#### Wiersema JR.

Attention-deficit/hyperactivity disorder (ADHD) is a prevalent life-span neurodevelopmental disorder characterised by age-inappropriate and persistent levels of hyperactivity, impulsivity and/or inattention, associated with significant impairments in a wide range of areas of everyday functioning. In the present symposium, we will present findings from recent studies that have applied different neuroscientific methods to better understand the basis of selfregulatory deficits in ADHD in order to guide therapeutic innovation. First, Jan R. Wiersema will give an introduction on the need for and the advantages of the use of cognitive neuroscience approaches to ADHD. Justina Sidlauskaite will present findings of an fMRI study on the neurobiological basis of state regulation in adults with ADHD. This will be followed by a talk by Monica Dhar that focuses on ERP correlates of cue processing and proactive cognitive control in adults with ADHD. Thereafter, Elke Godefroid will present ERP results of a study on salience processing in adults with ADHD and finally, Gabry Mies will demonstrate how pupil measurements can inform us about impaired mental effort allocation in adolescents with ADHD. Taken together, the symposiumillustrates the advantage of the use of different cognitive neuroscience approaches for a better understanding of selfregulatory deficits in ADHD, which may lead to urgently needed improvement of interventions

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Int J Psychophysiol. 2016;108:136-37.

MIRROR SYSTEM DEFICIT IN ADHD? STUDY OF MU RHYTHM SUPPRESSION DURING OBSERVATION AND IMITATION OF EMOTION-RELATED FACIAL MOVEMENTS.

## Lòpez V, Ortega R, Moenne C, et al.

Mu rhythm is an EEG oscillatory measure (9-13 Hz), whose suppression during movement execution or action observation is considered an indicator of the activity of the human analog of the mirror neuron system. Detection of facial emotional expressions involves detailed observation of facial movements. ADHD is known to be associated with social cognition impairments, including emotional face perception, theory of mind deficits and reduced empathy. The present work compared Mu suppression in 22 ADHD children and 18 matched control participants (32 % female, ages 9 to 14, Mean 10.8 SD: 1.5), while observing and later imitating the movements involved in the dynamic unfolding of facial emotion expressions. Participants observed and imitated facial expressions performed by actors in 96 short video clips, composed by two seconds of a neutral face and two seconds where a happy, sad, angry, or fear expression unfolded. The clip was preceded by a 1 second fixation cross and followed by a 1 second blank screen. In each trial, after the observation stage, they were asked for the presence of a specific emotion, (present in 50% of the trials). Then, they had to press a key to start co-acting the same facial movements. EEG (40 channels) was recorded using a NeuroScan NuAmps system. Eye movements were recorded using an Eyelink 1000 system. After artifact rejection, epochs of-500 ms to 3000 ms were extracted. The Morlets' wavelets procedure was used for time frequency analysis and a-500 to 0 ms window was used as a baseline for Z scoring. Change in power in the 9-13 Hz band during the 2000 ms window where movement occurred was used for statistical analysis. Results showed significant Mu suppression over central regions, more marked over the left hemisphere, during observation and imitation (F (1, 38) = 3.07, p < 0.05). Movement execution produced larger suppressions than observation in Controls. Suppression in the Control Group was significantly larger than in the ADHD group in both conditions (F (1, 18) = 6.68, p < 0.01) for all emotional expressions. Furthermore, observation and imitation did not significantly differed in the ADHD group. Nevertheless, when comparing the groups using only those trials in which a significant Mu suppression occurred no between groups

difference was observed. Lack of suppression in other networks has been reported in ADHD. This pattern is compatible with a functional, but not structural, deficit of the mirror system in ADHD

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Int J Psychophysiol. 2016;108:75.

EEG AND ERP CHARACTERISTICS OF ATTENTION DEFICIT HYPERACTIVITY DISORDER IN CHILDREN AND ADOLESCENTS.

#### Lazarev VV, Pontes M, Pontes AT, et al.

In search for psychophysiological correlates of Attention Deficit Hyperactivity Disorder (ADHD) that could contribute to elaboration of objective diagnostic approaches and reveal cerebral mechanisms underlying this type of neuropsychiatric disorder, various EEG methods combined with functional and behavioral testswere applied. In 32 boys suffering from ADHD (according to DSM-IVTR criteria) and 24 normally developing boys, aged 9-13 years, with I.Q. N 80 (WISC III), EEG signals were recorded at 20 scalp points in resting state, during intermittent photic stimulation (IPS) of 12 fixed frequencies of 3-27 Hz and during performance of the Attentional Network Test (ANT). In the spontaneous EEG of the resting state EEG, the ADHD patients showed 20% regional increase in delta and theta amplitude spectra in the frontal and left temporal areas. In the left temporal leads, augmented alpha amplitude spectra were also observed. During IPS, the driving amplitudes corroborated these results showing Γê+24% prevalence of the patients over controls in the left frontotemporal areas at the IPS frequencies corresponding to the delta and alpha bands. In addition, the patients had symmetric distribution of the photic driving while in the controls, significant right-side prevalence in the anterior regions was observed. Intrahemispheric EEG coherence in the ADHD patients during resting state and IPS showed relatively increased level in the left hemisphere in the delta, theta and alpha bands. The above-mentioned EEG results probably show relative inactivation of the frontal and left temporal cortex responsible for the voluntary attention concentration that is impaired in the ADHD. The ERP characteristics of the ADHD patients during ANT also showed significant decrease of the target late cognitive components in the left frontal and mid-frontal leads, and no difference between the groups in the right frontal, and all parietal and occipital points. Similarly, the cue late components in these patients were also reduced only in the frontal and frontopolar areas. These results corroborate the above conclusion regarding deficient prefrontal and frontal control functions in ADHD, accompanied by intact operational visuospatial functions of the posterior areas. In sum, the electrophysiological methods utilized in the present research look promising as complementary tools to determine objective biomarkers of ADHD

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Int J Psychophysiol. 2016;108:28.

#### MENTAL EFFORT IN ADOLESCENTS WITH ADHD.

## Mies GW, Moors P, Sonuga-Barke EJ, et al.

Mental effort plays an important role in theoretical models of ADHD; it is central to both motivational and cognitive-energetic accounts, but it has been underspecified and under-examined empirically. It could however, provide the missing link between task performance of difficult and challenging tasks requiring cognitive control, and the effects of extrinsic rewards on performance in ADHD. In this exploratory study we examined two putative effort-related deficits in ADHD; First, impairments in the ability to apply effort and second, alterations in effort-related decision making due to an altered cost-benefit analysis relating to the application of effort. For this purpose, we examined 1) performance on anN-back taskwith five levels of difficulty (1-, 2-, 3-, 4-, 5-back) and choice behavior on a subsequent effort discounting task, 2) pupil dilation during the N-back task, and 3) subjective measures of mental demand and effort application during the N-back task. Fifteen boys with ADHD and 16 controls (aged 12-17 years) participated in this study. Results showed that with increasing level of N-back difficulty, performance deteriorated, and participants with ADHD performed significantly worse than controls, independent of level of difficulty. In the effort-discounting task, however, nomain effect of group was found, indicating that adolescents with ADHD did not devalue effort-related rewards more than controls. This suggests that they are not more effort averse than controls. The overall pattern of pupil responses during theNback blocks looked similar for ADHD and control participants:

there was an initial increase in pupil dilation in the first 3-6 trials of a task block, afterwhich a gradual decline in pupil response occurred back to baseline. In the control group, the peak of this pupil dilation increased with level of difficulty up to 3-back, while in the ADHD group such an effect was absent. Finally, groups did not differ in the subjective experience of the mental demand of the different levels of the N-back task, nor in effort application. Together, these results suggest that performance decrements in ADHD in a working memory task such as the task used here might be related to a suboptimal application of mental effort, which is not reflected in subjective experiences, and subsequently does not appear to lead to an altered cost-benefit analysis related to the application of effort

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Isr Med Assoc J. 2018;20:373-78.

MEDICAL, COGNITIVE, AND PSYCHIATRIC CHARACTERISTICS IN A LARGE ISRAELI COHORT OF INDIVIDUALS WITH WILLIAMS SYNDROME.

Dror C, Sinai A, Gothelf D.

**Background**: Williams syndrome (WS) is a neurogenetic syndrome characterized by a variety of medical conditions and cognitive deficits along with distinct psychiatric and behavioral characteristics. To the best of our knowledge, no studies to date have comprehensively reported the prevalence of medical, cognitive deficits, and psychiatric disorders in one cohort of people with WS in one study.

**Objectives**: To detail the prevalence of the various clinical features of WS in a large nationwide Israeli cohort. To examine potential risk factors for attention deficit hyperactivity disorder (ADHD) in WS.

**Methods**: We investigated the effects of cardiovascular anomalies, intellectual quotient (IQ), and phonophobia (fear of sounds) on the likelihood of ADHD. The study included 80 participants with WS (mean age 7.76 years). Relevant medical information from medical records was obtained retrospectively. In addition, IQ testing and psychiatric assessments using structured tools were conducted. The association between ADHD and cardiovascular anomalies, IQ, and phonophobia was analyzed using a logistic regression.

**Results**: Supravalvular aortic stenosis and supravalvular pulmonary stenosis are the prevalent cardiovascular anomaly in WS. Phonophobia and ADHD are the most prevalent psychiatric diagnoses in people with WS. Phonophobia was significantly associated with the risk for ADHD in WS participants.

**Conclusions**: Our findings regarding the type and prevalence of medical, cognitive, and psychiatric characteristics in WS correspond to results in previous publications. We also showed a potential link between phonophobia and ADHD that merits further research

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J Korean Med Sci. 2018 Jan;33:e17.

COGNITIVE FUNCTION AND NEUROPSYCHOLOGICAL COMORBIDITIES IN CHILDREN WITH NEWLY DIAGNOSED IDIOPATHIC EPILEPSY.

Lee SY, Park JH, Park SJ, et al.

**BACKGROUND**: In this study, we aimed to identify cognitive function and neuropsychological comorbidities in children with newly diagnosed idiopathic epilepsy.

**METHODS**: We retrospectively reviewed the records of 97 antiepileptic drug-naive children (9.7 +/- 2.9 years; 54 males and 43 females) with newly diagnosed idiopathic epilepsy, all of whom underwent a neuropsychological battery. The battery consisted of the Korean Wechsler Intelligence Scale, Attention Deficit Hyperactivity Disorder (ADHD) Rating Scale, ADHD Diagnostic System, Children's Depression Inventory, and State-Trait Anxiety Inventory for Children. We investigated association between scores of the neuropsychological battery and epilepsy classification, lateralization of interictal epileptiform discharges (IEDs) on electroencephalography (EEG), and variables related to seizures.

**RESULTS**: Thirteen patients (14.3%) had ADHD symptoms. Three patients (4.1%) had depressive symptoms, and 9 (12.3%) had anxiety symptoms. Patients with idiopathic generalized epilepsy (IGE) had significantly lower full-scale intelligence and performance intelligence quotient scores than patients with idiopathic localization-related epilepsy (ILRE) (89.0 +/- 17.6 vs. 96.3 +/- 14.8; P = 0.030 and 88.9 +/- 16.3 vs. 97.0 +/- 16.4; P = 0.016, respectively). Patients with ILRE having unilateral IEDs had significantly higher full-

scale intelligence quotient scores than patients with ILRE having bilateral IEDs and patients with IGE (99.9  $\pm$  12.2 vs. 93.7  $\pm$  16.1 vs. 89.0  $\pm$  17.6; P = 0.039, respectively).

**CONCLUSION**: Our results suggest that idiopathic epilepsy may be accompanied by various neuropsychological comorbidities even at initial diagnosis. Patients with IGE and ILRE having bilateral IEDs on EEG appear more likely to be at high risk of decreased cognitive function

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J Nutr. 2018 Feb;148:227-35.

OMEGA-3 AND OMEGA-6 FATTY ACID SUPPLEMENTATION MAY REDUCE AUTISM SYMPTOMS BASED ON PARENT REPORT IN PRETERM TODDLERS.

Keim SA, Gracious B, Boone KM, et al.

**Background**: Children born preterm are at increased risk of autism spectrum disorder (ASD). n-3 (omega-3) Combined with n-6 (omega-6) fatty acids including gamma-linolenic acid (GLA) may benefit children born preterm showing early signs of ASD. Previous trials have reported that docosahexaenoic acid (DHA) promotes cognitive development in preterm neonates and n-3 fatty acids combined with GLA improve attention-deficit-hyperactivity disorder.

**Objectives**: The objectives of the pilot Preemie Tots Trial were 1) to confirm the feasibility of a full-scale trial in toddlers born very preterm and exhibiting ASD symptoms and 2) to explore the effects of supplementation on parent-reported ASD symptoms and related behaviors. Methods: This was a 90-d randomized, fully blinded, placebo-controlled trial in 31 children 18-38 mo of age who were born at </=29 wk of gestation. One group was assigned to daily Omega-3-6-9 Junior (Nordic Naturals, Inc.) treatment (including 338 mg eicosapentaenoic acid, 225 mg DHA, and 83 mg GLA), and the other group received canola oil (124 mg palmitic acid, 39 mg stearic acid, 513 mg linoleic acid, 225 mg alpha-linolenic acid, and 1346 mg oleic acid). Mixed-effects regression analyses followed intent-to-treat analysis and explored effects on parent-reported ASD symptoms and related behaviors.

**Results**: Of 31 children randomly assigned, 28 had complete outcome data. After accounting for baseline scores, those assigned to treatment exhibited a greater reduction in ASD symptoms per the Brief Infant Toddler Social Emotional Assessment ASD scale than did those assigned to placebo (difference in change = - 2.1 points; 95% CI: - 4.1, - 0.2 points; standardized effect size = - 0.71). No other outcome measure reflected a similar magnitude or a significant effect.

**Conclusions**: This pilot trial confirmed adequate numbers of children enrolled and participated fully in the trial. No safety concerns were noted. It also found clinically-significant improvements in ASD symptoms for children randomly assigned to receive Omega-3-6-9 Junior, but effects were confined to one subscale. A future full-scale trial is warranted given the lack of effective treatments for this population. This trial was registered at www.clinicaltrials.gov as NCT01683565

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J Pediatr Orthop. 2018 Mar;38:152-56.

TOE WALKING: A NEUROLOGICAL PERSPECTIVE AFTER REFERRAL FROM PEDIATRIC ORTHOPAEDIC SURGEONS. Haynes KB, Wimberly RL, VanPelt JM, et al.

**BACKGROUND**: Toe walking (TW) in children is often idiopathic in origin. Our purpose was to determine the incidence of a neurological etiology for TW in patients seen in the neurology clinic after referral from pediatric orthopaedic surgeons.

**METHODS**: We performed an Institutional Review Board approved retrospective review of 174 patients referred to the neurology clinic from orthopaedic surgeons at an academic pediatric tertiary care center between January 2010 and September 2015. Medical records were reviewed and data recorded including pertinent family history, birth history, age of initial ambulation, physical examination findings, and workup results including neuroimaging, neurophysiological studies, and findings of genetic testing and tissue biopsy. **RESULTS**: Sixty-two percent (108/174) of patients were found to have a neurological etiology for TW. Final pathologic diagnoses were: 37% (40/108) previously undiagnosed cerebral palsy (CP), 16.7% (18/108) peripheral neuropathy, 15.7% (17/108) autism spectrum disorder, 13.9% (15/108) hereditary spastic

paraparesis, 8.3% (9/108) attention deficit hyperactivity disorder, 5.6% (6/108) syndromic diagnosis, and 2.8% (3/108) spinal cord abnormality. Ankle equinus contractures were noted in idiopathic and neurological patients and did not indicate a pathologic origin. Seventy-one percent of unilateral toe walkers and 32% of bilateral but asymmetric toe walkers were diagnosed with CP (P<0.001). Twenty-six percent of 145 brain magnetic resonance imaging studies diagnosed CP. Of the 125 (72%) with spinal imaging, 3 had spinal pathology to account for TW. Fourteen percent of 87 subjects with an electromyography/nerve conduction study had abnormal results indicating a peripheral polyneuropathy.

**CONCLUSIONS**: An underlying pathologic diagnosis was found in 62% of patients referred to neurology for TW. A concerning birth history, delayed initial ambulation, unilateral TW, upper or lower motor neuron signs on examination, or behavioral features may suggest a pathologic diagnosis. Ankle contracture is not predictive of an abnormal diagnosis and can be found in idiopathic patients. CP, peripheral neuropathy, autism spectrum disorder, and hereditary spastic paraparesis are the most common pathologic diagnoses identified in our population. **LEVEL OF EVIDENCE**: Level III-retrospective cohort

JAMA. 2018 Jul;320:16-18.  ADAM GAZZALEY, MD, PHD: DEVELOPING PRESCRIBABLE VIDEO GAMES.  Abbasi J.
JAMA. 2018 Jul;320:237-39.  DIGITAL MEDIA AND SYMPTOMS OF ATTENTION-DEFICIT/HYPERACTIVITY DISORDER IN ADOLESCENTS.  Radesky J.

JAMA Pediatr. 2018;172:670-77.

ASSOCIATION OF EXPOSURE TO DIETHYLSTILBESTROL DURING PREGNANCY WITH MULTIGENERATIONAL NEURODEVELOPMENTAL DEFICITS.

Kioumourtzoglou M-A, Coull BA, O'Reilly EJ, et al.

**Importance**: Animal evidence suggests that endocrine disruptors affect germline cells and neurodevelopment. However, to date, the third-generation neurodevelopmental outcomes in humans have not been examined.

**Objective**: To explore the potential consequences of exposure to diethylstilbestrol or DES across generations-specifically, third-generation neurodevelopment.

**Design, Setting, and Participants**: This cohort study uses self-reported health information, such as exposure to diethylstilbestrol during pregnancy and attention-deficit/hyperactivity disorder (ADHD) diagnosis, from 47 540 participants enrolled in the ongoing Nurses' Health Study II. The 3 generations analyzed in this study were the participants (F1 generation), their mothers (F0 generation), and their live-born children (F2 generation).

**Main Outcomes and Measures**: Participant- and mother-reported exposure to diethylstilbestrol during pregnancy and physician-diagnosed child ADHD. Results: The total number of women included in this study was 47 540. Of the 47 540 F0 mothers, 861 (1.8%) used diethylstilbestrol and 46 679 (98.2%) did not while pregnant with the F1 participants. Use of diethylstylbestrol by F0 mothers was associated with an increased risk of ADHD among the F2 generation: 7.7% vs 5.2%, adjusted odds ratio (OR), 1.36 (95%CI, 1.10-1.67) and an OR of 1.63 (95%CI, 1.18-2.25) if diethylstilbestrol was taken during the first trimester of pregnancy. No effect modification was observed by the F2 children's sex.

**Conclusions and Relevance**: This study provides evidence that diethylstilbestrol exposure is associated with multigenerational neurodevelopmental deficits. The doses and potency level of environmental endocrine

disruptors to which humans are exposed are lower than those of diethylstilbestrol, but the prevalence of such exposure and the possibility of cumulative action are potentially high and thus warrant consideration

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J Abnorm Child Psychol. 2018 May;46:659-69.

EVIDENCE FOR THE TRAIT-IMPULSIVITY ETIOLOGICAL MODEL IN A CLINICAL SAMPLE: BIFACTOR STRUCTURE AND ITS RELATION TO IMPAIRMENT AND ENVIRONMENTAL RISK.

## Rodenacker K, Hautmann C, Görtz-Dorten A, et al.

The trait-impulsivity etiological model assumes that a general factor (trait-impulsivity) underlies attention-deficit/hyperactivity disorder (ADHD), oppositional defiant disorder (ODD), and other externalizing disorders. We investigated the plausibility of this assumption by testing the factor structure of ADHD and ODD in a bifactor framework for a clinical sample of 1420 children between 6 and 18 years of age (M = 9.99, SD = 3.34; 85% male). Further, the trait-impulsivity etiological model assumes that ODD emerges only if environmental risk factors are present. Our results support the validity of the trait-impulsivity etiological model, as they confirm that ADHD and ODD share a strong general factor of disruptive behavior (DB) in this clinical sample. Furthermore, unlike the subdimensions of ADHD, we found that the specific ODD factor explained as much true score variance as the general DB factor. This suggests that a common scale of ADHD and ODD may prove to be as important as a separate ODD subscale to assess externalizing problems in school-age children. However, all other subscales of ADHD may not explain sufficient true score variance once the impact of the general DB factor has been taken into consideration. In accordance with the trait-impulsivity model, we also showed that all factors, but predominantly the general factor and specific inattention factor, predicted parent-rated impairment, and that predominantly ODD and impulsivity are predicted by environmental risk factors

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J Abnorm Child Psychol. 2018 May;46:729-39.

PATHWAYS FROM BIRTH WEIGHT TO ADHD SYMPTOMS THROUGH FLUID REASONING IN YOUTH WITH OR WITHOUT INTELLECTUAL DISABILITY.

## Morgan JE, Lee SS, Loo SK, et al.

Although individual differences in fluid reasoning reliably mediate predictions of attention-deficit/hyperactivity disorder (ADHD) symptoms from birth weight in youth with typical cognitive development (TD), it is unknown if this indirect effect operates similarly in the development of ADHD symptoms secondary to intellectual disability (ID). Thus, we evaluated mediation by fluid reasoning in a longitudinal sample of 163 youth (45% female) with (n = 52) or without (n = 111) ID who were followed prospectively from age 5 to age 13. At age 9, youth completed the Arithmetic subtest of the Wechsler Intelligence Scale for Children, a measure of fluid reasoning. At ages 9 and 13, mothers and teachers separately rated youth ADHD symptoms and mothers completed a diagnostic interview. Mediation was tested via path analysis with bootstrapped confidence intervals, and moderated mediation estimated whether indirect effects differed between ID and TD youth or based on youth IQ. Controlling for demographic factors and age 9 ADHD symptoms, age 9 Arithmetic mediated birth weight and multi-method/informant age 13 ADHD symptoms, such that birth weight positively predicted Arithmetic, which negatively predicted ADHD symptoms. Neither ID status nor IQ moderated the observed indirect effect through Arithmetic, suggesting that it was similar for ID and TD youth as well as across the range of youth IQs. These findings support previous evidence that fluid reasoning, as measured by Arithmetic, may causally mediate birth weight and ADHD symptoms, and suggest that this pathway operates similarly with respect to the development of ADHD symptoms in youth with ID

J Abnorm Child Psychol. 2018 Jul;46:951-63.

IS THE ASSOCIATION OF ADHD WITH SOCIO-ECONOMIC DISADVANTAGE EXPLAINED BY CHILD COMORBID EXTERNALIZING PROBLEMS OR PARENT ADHD?

Miller LL, Gustafsson HC, Tipsord J, et al.

It has been unclear whether an associations of child ADHD with socio-economic disadvantage (SES) could be accounted for by (a) parental ADHD explaining both low SES and child ADHD, and/or (b) the joint overlap of ODD or CD with low SES and ADHD. Study 1 used a community-recruited case-control sample with detailed evaluation of SES indicators, child ADHD, child externalizing, and parent ADHD symptoms (n = 931 children, 521 ADHD, 577 boys, 354 girls) in a path modeling analysis with latent variables. Study 2 evaluated ADHD and externalizing behavior in a regression model using a poverty index for SES, in 70,927 children (48.2% female) aged 5-17 years from the US 2011-2012 National Survey of Children's Health (NSCH). In Study 1, lower SES was related to the ADHD latent variable,  $\beta = -.18$ , p < .001; 95%CI [-.25,-.12]. This effect held when parent ADHD and child ODD and CD were in the model,  $\beta = -.11$ , p < .01, 95% CI [-.09,-.03], equivalent to OR = 1.50, 95% CI[1.12-2.04]). In Study 2, these results replicated. Adjusting only for age and sex, children from families who were below 200% of the federal poverty line were more likely to have moderate or severe ADHD than no ADHD, versus children above that line, OR = 2.13, 95% CI[1.79,2.54], p < .001. The effect held after adjusting for disruptive/externalizing problems, OR = 1.61, p < .01, 95%CI [1.32,1.96]. The effect size for comparable models was similar across both studies, lending higher confidence to the results. It is concluded that the SES association with child ADHD is not explained by artifact and requires a mechanistic explanation

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J Abnorm Child Psychol. 2018 May;46:671-83.

LONGITUDINAL ASSOCIATIONS OF PARENTAL EMOTION SOCIALIZATION AND CHILDREN€™S EMOTION REGULATION: THE MODERATING ROLE OF ADHD SYMPTOMATOLOGY.

### Breaux RP, McQuade JD, Harvey EA, et al.

Theory and research suggest that parents reactions to children s emotions play a critical role in teaching children effective emotion regulation (ER) skills, but no studies have directly examined the role that parent emotion socialization plays in the development of ER in children with ADHD. Gaining insight into the causes of impaired ER, particularly in youth with ADHD who are known to have poor ER, has important theoretical and translational significance. The present study is the first to longitudinally examine whether emotion socialization predicts later physiological and adult-reported measures of ER in children with and without ADHD. It also sought to determine if these relations are moderated by ADHD symptoms. Participants were 61 children (31 girls, 30 boys; M = 10.67 years, SD = 1.28) with and without clinically significant ADHD symptoms. At Time 1, parent reports of emotion socialization and parent- and teacher-report of child ADHD symptoms were collected. At Time 2, child ER measures were collected based on parent- and teacher-report and physiological reactivity during an impossible puzzle and a social rejection task. Physiological measures included respiratory sinus arrhythmia and skin conductance level (SCL). Supportive parenting practices were associated with better parent-rated emotion regulation skills for all children and greater SCL reactivity for children with high ADHD symptoms. Non-supportive parenting reactions were associated with greater adultrated emotional lability for children with high ADHD symptoms. Results highlight the importance of considering multiple aspects of ER, including physiological manifestations. Findings suggest that parents' use of adaptive emotion socialization practices may serve as a protective factor for children's ER development and may be particularly critical for youth with ADHD. Our findings support the use of interventions addressing parent emotion socialization to help foster better ER in children

J Abnorm Child Psychol. 2018 May;46:701-11.

PROCESSING SPEED PREDICTS BEHAVIORAL TREATMENT OUTCOMES IN CHILDREN WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER PREDOMINANTLY INATTENTIVE TYPE.

## Adalio CJ, Owens EB, McBurnett K, et al.

Neuropsychological functioning underlies behavioral symptoms of attention-deficit/hyperactivity disorder (ADHD). Children with all forms of ADHD are vulnerable to working memory deficits and children presenting with the inattentive form of ADHD (ADHD-I) appear particularly vulnerable to processing speed deficits. As ADHD-I is the most common form of ADHD presented by children in community settings, it is important to consider how treatment interventions for children with ADHD-I may be affected by deficits in processing speed and working memory. We utilize data collected from 199 children with ADHD-I, aged 7 to 11 years, who participated in a randomized clinical trial of a psychosocial-behavioral intervention. Our aims are first to determine whether processing speed or working memory predict treatment outcomes in ADHD-I symptom severity, and second whether they moderate treatment effects on ADHD-I symptom severity. Results of linear regression analyses reveal that baseline processing speed significantly predicts posttreatment ADHD-I symptom severity when controlling for baseline ADHD-I symptom severity, such that better processing speed is associated with greater symptom improvement. However, predictive effects of working memory and moderation effects of both working memory and processing speed are not supported in the present study. We discuss study limitations and implications of the relation between processing speed and treatment benefits from psychosocial treatments for children with ADHD-I

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J Abnorm Child Psychol. 2018 May;46:713-27.

INATTENTIVE BEHAVIOR IN BOYS WITH ADHD DURING CLASSROOM INSTRUCTION: THE MEDIATING ROLE OF WORKING MEMORY PROCESSES.

## Orban SA, Rapport MD, Friedman LM, et al.

Children with ADHD exhibit clinically impairing inattentive behavior during classroom instruction and in other cognitively demanding contexts. However, there have been surprisingly few attempts to validate anecdotal parent/teacher reports of intact sustained attention during â€~preferred' activities such as watching movies. The current investigation addresses this omission, and provides an initial test of how ADHD-related working memory deficits contribute to inattentive behavior during classroom instruction. Boys ages 8â€"12 (M = 9.62, SD = 1.22) with ADHD (n = 32) and typically developing boys (TD; n = 30) completed a counterbalanced series of working memory tests and watched two videos on separate assessment days: an analogue math instructional video, and a non-instructional video selected to match the content and cognitive demands of parent/teacher-described preferred activities. Objective, reliable observations of attentive behavior revealed no between-group differences during the non-instructional video (d = â^0.0.02), and attentive behavior during the non-instructional video was unrelated to all working memory variables (r = â"0.11 to 0.19, ns). In contrast, the ADHD group showed disproportionate attentive behavior decrements during analogue classroom instruction (d = â^0.71). Bias-corrected, bootstrapped, serial mediation revealed that 59% of this between-group difference was attributable to ADHD-related impairments in central executive working memory, both directly (ER = 41%) and indirectly via its role in coordinating phonological short-term memory (ER = 15%). Between-group attentive behavior differences were no longer detectable after accounting for ADHD-related working memory impairments (d = \( \hat{a}^0.29, \text{ ns} \)). Results confirm anecdotal reports of intact sustained attention during activities that place minimal demands on working memory, and indicate that ADHD children's inattention during analogue classroom instruction is related, in large part, to their underdeveloped working memory abilities

J Abnorm Child Psychol. 2018 May;46:685-99.

WITHIN-FAMILY EFFECTS OF SMOKING DURING PREGNANCY ON ADHD: THE IMPORTANCE OF PHENOTYPE.

## Marceau K, Cinnamon Bidwell L, Karoly HC, et al.

We sought to test within- and between- family associations of smoking during pregnancy (SDP) and attention deficit-hyperactivity disorder (ADHD) symptoms using a structured interview based on the conventional Diagnostic and Statistical Manual of Mental Disorders, 4th edition (DSM-IV) symptoms and the Strengths and Weaknesses of ADHD-Symptoms and Normal-Behavior (SWAN) scale, which is a population based measure that grew out of the notion that an ADHD diagnosis exists on the extreme end of a continuum of normative behaviors and includes both above- and below- average performance on attention and activity. We used a sibling-comparison approach in a sample of 173 families including siblings aged 7â€"16 vears (52% male) drawn from the state of Missouri, USA, wherein mothers smoked during one pregnancy but not the other. There was a within-family effect of smoking during pregnancy on SWAN hyperactivity/impulsivity and SWAN total ADHD behaviors. The associations between SDP and DSM-IV-based ADHD symptom dimensions as well as SWAN inattention were explained by familial confounds. These findings suggest that SDP exerts a potentially causal effect on increased ADHD hyperactive/impulsive behaviors and that this SDP effect is best captured when hyperactivity/impulsivity is assessed more normatively across the population, rather than specifically assessing problematic behaviors via DSM symptoms. Thus, any potentially causal effect of SDP on ADHD symptom dimensions may be restricted to hyperactive/impulsive behaviors rather than inattention, and normative, non-DSM-IV based behavioral measures may provide a more sensitive test of mechanisms of SDP-ADHD symptom associations, particularly in non-clinical samples

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J Abnorm Psychol. 2018;127:529-39.

TESTING FORMAL PREDICTIONS OF NEUROSCIENTIFIC THEORIES OF ADHD WITH A COGNITIVE MODEL-BASED APPROACH.

### Weigard A, Huang-Pollock C, Brown S, et al.

Neuroscientific theories of attention-deficit/hyperactivity disorder (ADHD) alternately posit that cognitive aberrations in the disorder are due to acute attentional lapses, slowed neural processing, or reduced signal-to-noise ratios. However, they make similar predictions about behavioral summary statistics (response times [RTs] and accuracy), hindering the field's ability to produce strong and specific tests of these theories. The current study uses the linear ballistic accumulator (LBA; Brown & Heathcote, 2008), a mathematical model of choice RT tasks, to distinguish between competing theory predictions. Children with ADHD (n = 80) and age-matched controls (n = 32) completed a numerosity discrimination paradigm at 2 levels of difficulty, and RT data were fit to the LBA model to test theoretical predictions. Individuals with ADHD displayed slowed processing of evidence for correct responses (signal) relative to their peers but comparable processing of evidence for error responses (noise) and between-trial variability in processing (performance lapses). The findings are inconsistent with accounts that posit an increased incidence of attentional lapses in the disorder and provide partial support for those that posit slowed neural processing and lower signal-to-noise ratios. Results also highlight the utility of well-developed cognitive models for distinguishing between the predictions of etiological theories of psychopathology

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J Adolesc Health. 2018.

RISK OF TRAUMATIC BRAIN INJURY AMONG CHILDREN, ADOLESCENTS, AND YOUNG ADULTS WITH ATTENTION-DEFICIT HYPERACTIVITY DISORDER IN TAIWAN.

Liou Y-J, Wei H-T, Chen M-H, et al.

**Purpose**: Previous studies suggested that patients with attention-deficit hyperactivity disorder (ADHD) were prone to health-risk behaviors and accidents. However, the relationship of ADHD with the risk of traumatic brain injury (TBI) remained uncertain.

**Methods**: Using the Taiwan National Health Insurance Research Database, 72,181 children (aged 3-11 years), adolescents (12-17 years), and young adults (18-29 years) with ADHD and 72,181 age-/sex-matched

controls were enrolled between 2001 and 2009, and followed up to the end of 2011 in our study. Those who developed any TBI during the follow-up period were identified.

**Results**: Children, adolescents, and young adults with ADHD had a higher incidence of developing any TBI (9.8% vs. 2.2%, p < .001), such as skull fracture (.2% vs. .1%, p < .001) and concussion (4.3% vs. 1.0%, p < .001), than the controls did. Cox regression analysis with the adjustment of demographic data, psychiatric comorbidities, and ADHD medications showed that ADHD was related to an increased risk of subsequent TBI (hazard ratio: 4.57, 95% confidence interval: 4.31 $\Gamma$ Çô4.85), and indicated that long-term use of ADHD medication was associated with a reduced likelihood of subsequent TBI (hazard ratio: .93, 95% confidence interval: .87-.99).

**Conclusions**: Patients with ADHD had an increased risk of developing any TBI compared with the controls. Long-term use of ADHD medications would reduce this risk. Our findings suggested that the public health government and clinicians should pay more attention to the TBI risk among patients with ADHD, and further indicated the importance of the optimal treatment for ADHD

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J Autism Dev Disord. 2018;1-8.

TIMING OF THE DIAGNOSES OF ATTENTION DEFICIT HYPERACTIVITY DISORDER AND AUTISM SPECTRUM DISORDER IN TAIWAN.

### Wei H-T, Hsu J-W, Huang K-L, et al.

ADHD comorbidity has been associated with delayed diagnosis of ASD, but no study has investigated this association in an Asian country. Children with ASD were included and divided into three groups: ADHD before ASD, ADHD same/after ASD, and ASD only. Timing of ASD and ADHD diagnoses were assessed. The logistic regression model was performed to investigate the likelihood of being diagnosed with ASD after 6 years of age between three groups. ADHD before ASD (OR 10.93) group was more likely to being diagnosed with ASD after 6 years of age compared with ADHD same/after ASD (OR: 1.37) and ASD only groups. ADHD comorbidity would delay the diagnosis of ASD in the general clinical settings in Taiwan

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J Autism Dev Disord. 2018;48:2758-65.

FACE IDENTITY RECOGNITION AND THE SOCIAL DIFFICULTIES COMPONENT OF THE AUTISM-LIKE PHENOTYPE: EVIDENCE FOR PHENOTYPIC AND GENETIC LINKS.

### Lewis GJ, Shakeshaft NG, Plomin R.

Autism spectrum disorder (ASD) and autism-like traits are associated with deficits in face memory ability, although it is not yet clear whether this deficit reflects a specific aspect of the ASD/autism-like phenotype. We addressed this issue using a neurotypical sample of adolescent twins (Ncomplete pairs = 782) drawn from the Twins Early Development Study who were assessed on face and object memory performance alongside two core aspects of autism-like traits: (i) difficulties with social behavior/interactions, and (ii) attention to detail. We observed a negative association between face memory ability and difficulties with social behavior/interactions. This association reflected an overlapping genetic etiology: heritable influences acting on face memory ability are associated with the social difficulties aspects of autism-like traits

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Journal of Behavioral Addictions. 2018;7:284-91.

OPPOSITIONAL DEFIANT DISORDER/CONDUCT DISORDER CO-OCCURRENCE INCREASES THE RISK OF INTERNET ADDICTION IN ADOLESCENTS WITH ATTENTION-DEFICIT HYPERACTIVITY DISORDER.

Gunes H, Tanidir C, Adaletli H, et al.

**Objectives**: The aims of this cross-sectional study were to assess the prevalence of Internet addiction (IA) in a clinical sample of adolescents with attention-deficit hyperactivity disorder (ADHD) and to detect the moderating effects of co-occurring oppositional defiant disorder/conduct disorder (ODD/CD) on the association between ADHD and IA.

**Methods**: The study group comprised 119 adolescent subjects who were consecutively referred to our outpatient clinic with a diagnosis of ADHD. The Turgay DSM-IV-Based Child and Adolescent Disruptive Behavioral Disorders Screening and Rating Scale (T-DSM-IV-S) was completed by parents, and subjects were asked to complete the Internet Addiction Scale (IAS).

**Results**: The IAS results indicated that 63.9% of the participants (n = 76) fell into the IA group. Degree of IA was correlated with hyperactivity/impulsivity symptoms but not with inattention symptoms. As compared to the ADHD-only group (without comorbid ODD/CD), ADHD + ODD/CD subjects returned significantly higher scores on the IAS.

**Conclusions**: As adolescents with ADHD are at high risk of developing IA, early IA detection and intervention is of great importance for this group. In addition, adolescents with ADHD + ODD/CD may be more vulnerable to IA than those in the ADHD-only group and may need to be more carefully assessed for IA

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Journal of Biotechnology. 2017;256:S78.

THE MICRODELETION OF 15 Q 11.2 LOCUS ENCOMPASSING TUBGCP5, NIPA1, NIPA2, AND CYFIP1 GENES IN AN EPILEPTIC CASE WITH MACROCEPHALY, ATTENTION-DEFICIT/HYPERACTIVITY DISORDER (ADHD), SPEECH AND MOTOR DELAY.

### Ozdemir O, Yildiz O, Karakaya T, et al.

Chromosome 15q11.2 deletion syndrome (OMIM#615656) is a contiguous gene deletion syndrome flanked by BP1 and BP2 of the Prader-Willi/Angelman syndrome critical region with comprising approximately 300-500 kb. Here we report a case of various phenotypic spectrum with TUBGCP5, NIPA1, NIPA2, and CYFIP1 genes deletion. We report a non-consanguineous 17-year-old female patient with macrocephaly, dysmorphic facial traits, as well as developmental delay, intellectual disability, attention-deficit/hyperactivity disorder (ADHD) and epilepsy in the current case report. She was in a normal karyotype but 315 kb deletion at 15q11.2 BP1 and BP2 locus that encompassed TUBGCP5 NIPA1, NIPA2, and CYFIP1 genes were detected after MicroArray-CGH (Agilent 60 K platform, US) analysis. Based on the current case report, we confirmed that the clinical spectrum of epilepsy, speech and psychomotor developmental delay, autism, macrocephaly and attention-deficit/hyperactivity maybe associated with 15q11.2 BP1 BP2 microdeletion locus due to haploinsufficiency for without Prader-Willi/Angelman syndrome

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J Child Adolesc Psychopharmacol. 2018;28:415-22.

USE AND CHARACTERISTICS OF ANTIPSYCHOTIC/METHYLPHENIDATE COMBINATION THERAPY IN CHILDREN AND ADOLESCENTS WITH A DIAGNOSIS OF ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.

## Scholle O, Banaschewski T, Enders D, et al.

**Objective**: Children and adolescents with attention-deficit/hyperactivity disorder (ADHD) frequently have comorbidities that are potential indications for antipsychotics (APs). Some studies have suggested that the combined use of methylphenidate (MPH) and APs is increasing in this population group. Longitudinal analyses and in-depth investigations on the substance level are lacking. This study aimed to estimate the cumulative proportion of concomitant AP/MPH use in children and adolescents with ADHD over a follow-up of up to 9 years and to describe patient characteristics stratified by specific AP drug.

**Methods**: Based on claims data, concomitant AP/MPH use was identified among 67,595 children and adolescents with ADHD starting MPH treatment between 2005 and 2013. Characteristics and diagnoses-including those indicating appropriateness of AP use according to approved indications and/or guidelines-were examined at the time of first AP/MPH combination therapy. In addition, subsequent use of AP/MPH combination therapy was evaluated.

**Results**: The cumulative proportion of individuals with any AP/MPH combination therapy rose to over 6% within 9 years after initiating MPH. The most frequent APs first used in combination with MPH were risperidone (72%), pipamperone (15%), and tiapride (8%). Percentages of psychiatric hospitalization in the year preceding the first combination therapy with MPH were 33%, 43%, and 19%, respectively. The

Newsletter – ADHD luglio 2018

proportion of individuals with potentially appropriate use was high (>72%) in risperidone/MPH and tiapride/MPH and low (15%) in pipamperone/MPH combination users. Conduct disorders and tic disorders were frequent in users who were prescribed MPH with risperidone and tiapride, respectively. One-quarter of patients with AP/MPH combination therapy were one-time-only combination users.

**Conclusion**: Our study suggests that a considerable proportion of children and adolescents with ADHD receive MPH in combination with APs and that this is a factor not only during the first years of MPH treatment. ADHD guidelines should specify algorithms concerning the use of AP medication

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J Child Psychol Psychiatry. 2018 May;59:556-64.

FORMING FIRST IMPRESSIONS OF CHILDREN: THE ROLE OF ATTENTION€● DEFICIT/HYPERACTIVITY DISORDER SYMPTOMS AND EMOTION DYSREGULATION.

Lee CA, Milich R, Lorch EP, et al.

**Background**: Previous research on peer status of children with attention-deficit/hyperactivity disorder (ADHD) has focused on already-established peer groups, rendering the specific social behaviors that influence peers initial impressions largely unknown. Recently, theorists have argued that emotion dysregulation is a key aspect of ADHD, with empirical work finding relations between emotion dysregulation and social outcomes. Therefore, the current study focuses on the initial interactions among children varying in ADHD symptoms duringh a novel playgroup, proposing that emotion dysregulation displayed during the playgroup may serve as a possible pathway between ADHD symptoms and peers initial negative impressions.

**Methods**: Participants were 233 elementary-age children ranging from 8 to 10 years old (M = 8.83, 70% male). Parents and teachers rated children s ADHD symptoms and related impairment; 51% of the children met criteria for an ADHD diagnosis. Then, children participated with unfamiliar peers in a three-hour playgroup that included three structured and two unstructured tasks. After the tasks, children and staff rated each child on social outcomes. Coders unaware of child s diagnostic status watched videos of the groups and rated each child s global emotion dysregulation during each task.

**Results**: Using multiple raters and methods, ADHD severity was associated with more negative peer ratings, through observed emotion dysregulation. Results were consistent for both parent and teacher ratings of ADHD severity as well as for both peer ratings of likeability and staff ratings of perceived peer likeability.

**Conclusions**: When focusing on improving peers initial impressions of children with ADHD symptoms, emotion dysregulation may be a valuable target for intervention

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J Clin Psychiatry. 2018;79.

RISK OF TYPE 2 DIABETES IN ADOLESCENTS AND YOUNG ADULTS WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER: A NATIONWIDE LONGITUDINAL STUDY.

Chen M-H. Pan T-L. Hsu J-W. et al.

**Background**: Studies have suggested there is an association between attention-deficit/hyperactivity disorder (ADHD) and type 2 diabetes mellitus (DM)-related risk factors, such as obesity, hypertension, and dyslipidemia. However, the association between ADHD and type 2 DM remains unknown.

**Methods**: Using the Taiwan National Health Insurance Research Database, we enrolled 35,949 adolescents and young adults with ADHD (ICD-9-CM code: 314) and 71,898 (1:2) age- and sex-matched controls from 2002 through 2009 and followed up with them until the end of 2011. Participants who developed type 2 DM during the follow-up period were identified.

**Results**: Adolescents (hazard ratio [HR] = 2.83; 95% CI, 1.96-4.09) and young adults (HR = 3.28; 95% CI, 1.41-7.63) with ADHD had a higher risk of developing type 2 DM than did the controls after adjustment for demographic characteristics, use of ADHD medications and atypical antipsychotics, and medical comorbidities. Individuals with ADHD had a shorter mean -\ SD duration between enrollment and onset of type 2 DM (3.17 -\ 2.33 vs 4.08 -\ 2.11 years, P = .004) during the follow-up compared with the controls. Sensitivity analyses after excluding first-year (HR = 2.36; 95% CI, 1.65-3.38) and first-3-year (HR = 1.92;

95% CI, 1.19-3.09) observation periods were consistent. Long-term use of atypical antipsychotics was associated with a higher likelihood of subsequent type 2 DM (HR = 2.82, 95% CI, 1.74-4.58).

**Discussion**: Adolescents and young adults with ADHD were more likely than non-ADHD controls to develop type 2 DM in later life. In addition, those with ADHD taking atypical antipsychotics exhibited a higher risk. Although correlation does not equal causation, our findings merit further study about the relationship between ADHD and type 2 DM

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J Clin Psychopharmacol. 2018;38:407-09.

SUCCESSFUL ADD-ON VORTIOXETINE FOR AN ADOLESCENT WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER. *Naguy A, Alamiri B.* 

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J Am Acad Child Adolesc Psychiatry. 2018.

FACIAL EMOTION RECOGNITION AND EYE GAZE IN ATTENTION-DEFICIT/HYPERACTIVITY DISORDER WITH AND WITHOUT COMORBID CONDUCT DISORDER.

Airdrie JN, Langley K, Thapar A, et al.

**Objective**: Conduct disorder (CD) is associated with impairments in facial emotion recognition. However, CD commonly co-occurs with attention-deficit/hyperactivity disorder (ADHD); thus, it is unclear whether these impairments are explained by ADHD or by one of its core features inattention. We explored whether emotion recognition impairments are specific to individuals with ADHD and comorbid CD while also examining the mechanisms that might explain such deficits.

**Method**: A total of 63 male and female adolescents with ADHD (mean age = 14.2 years, age range = 11-18 years) and with (ADHD+CD) or without (ADHD) comorbid CD, and 41 typically developing controls (HC; mean age = 15.5, age range =  $11\Gamma$ Çô18 years) performed an emotion recognition task with concurrent eyetracking.

**Results**: Participants with ADHD+CD were less accurate at recognizing fear and neutral faces, and more likely to confuse fear with anger than participants with ADHD alone and HC. Both ADHD subgroups fixated the eye region less than HC. Although there was a negative correlation between ADHD symptom severity and eye fixation duration, only CD severity was inversely related to emotion recognition accuracy.

**Conclusion**: Only ADHD participants with comorbid CD showed impairments in emotion recognition, suggesting that these deficits are specific to individuals with conduct problems. However, lack of attention to the eye region of faces appears to be a characteristic of ADHD. These findings suggest that emotion recognition impairments in those with ADHD+CD are related to misinterpretation rather than poor attention, offering interesting opportunities for intervention

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J Am Acad Child Adolesc Psychiatry. 2018;57:481-90.

COGNITIVE-BEHAVIORAL THERAPY FOR CHILDREN WITH ANXIETY AND COMORBID ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.

Gould KL, Porter M, Lyneham HJ, et al.

**Objective**: To determine whether comorbid attention-deficit/hyperactivity disorder (ADHD) diagnosis (including subtype) predicts response to cognitive-behavior therapy (CBT) for anxiety in children and to examine change in ADHD symptoms after treatment of primary anxiety.

**Method**: A sample of 842 children 5 to 18 years of age received CBT for a primary anxiety disorder. A subsample of 94 children met criteria for comorbid mild-to-moderate ADHD, mostly consisting of predominantly inattentive (n = 61) and combined (n = 27) subtypes. Outcome was defined as response (change in diagnostic severity) and remission (absence of the primary diagnosis) at each time point (after treatment and 3- and/or 6-month follow-up) and analyzed using linear and logistic mixed models.

**Results**: Neither ADHD diagnosis nor subtype predicted response or remission rates for children's primary anxiety disorders. Children with ADHD also showed modest yet significant improvements in ADHD symptoms after CBT for anxiety.

**Conclusion**: The present findings support the suitability of manual-based group-based CBT for anxiety treatment in children with nonprimary ADHD. Further research should examine whether the positive outcomes reported can be extended to children with primary or severe ADHD

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Journal of the Intensive Care Society. 2018.

## A CASE OF SINUS PAUSE INDUCED BY SWALLOWING IN THE SETTING OF OLANZAPINE AND GUANFACINE OVERDOSE. Kolarich AR, Mubarak M, Wells S, et al.

Olanzapine, a second-generation antipsychotic, is used in both adult and pediatric populations for schizophrenia, bipolar disorder, and depression and has been associated with autonomic dysregulation in the setting of overdose. Guanfacine is a sympatholytic drug used in the treatment of attention deficit hyperactivity disorder and has also been associated with autonomic dysfunction. We present a unique case of a 17-year-old male who overdosed on 340 mg of olanzapine and 189 mg of extended-release guanfacine with a previously unreported adverse event. Specifically, five days after ingestion, he developed a  $5\Gamma$ Çô8 s sinus pause every time he forcefully swallowed any beverage, suggestive of a vagal hypersensitivity reaction. The report will review the autonomic dysfunction of olanzapine and guanfacine and management of asymptomatic sinus pause in the critical care setting

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Kind en Adolescent. 2018 May;39:143-59.

OUDERINTERVENTIE VOOR GEDRAGSPROBLEMEN BIJ KINDEREN: EVEN EFFECTIEF VOOR VERSCHILLENDE GEZINNEN? = PARENTING PROGRAMME FOR DISRUPTIVE CHILD BEHAVIOUR: EQUALLY EFFECTIVE FOR DIVERSE FAMILIES?

## Leijten P, Menting A, Wijngaards-de Meij L, et al.

Parenting programmes are an effective strategy for reducing children s behavioural problems. It is important to understand who benefits more from these programmes and who benefits less. There are trends that suggest that families with a migration background or lower levels of education are not referred to evidence-based programmes, based on the untested assumption that these programmes do not meet their needs. The same holds for families of children with co-occurring ADHD symptoms and emotional problems. A better understanding of who benefits from parenting programmes will allow more careful matching between families and programmes. We used data from 786 families (with children aged 2-10 years) from four trials in the Incredible Years parenting programme in the Netherlands. Of these families, 29 % had a migration background and 31 % had lower educational levels. Our findings show that Incredible Years reduced disruptive child behaviour. Effects did not differ between families with different migration or educational backgrounds, or between children showing more or fewer ADHD symptoms. Children with more severe disruptive behaviour and children with more emotional problems benefited more in terms of reduced disruptive child behaviour. Thus the parenting programme yielded similar benefits for families with diverse backgrounds

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Kindheit und Entwicklung: Zeitschrift Klinische Kinderpsychologie. 2018 Jul;27:165-74.

INTELLIGENZDIAGNOSTIK BEI KINDERN UND JUGENDLICHEN MIT ADHS: EINE ANALYSE DER WISC-V-LEISTUNGSPROFILE. = MEASURING INTELLECTUAL PERFORMANCES OF CHILDREN AND ADOLESCENTS WITH ADHD: AN ANALYSIS OF THE WISC-V PROFILES.

## Pauls F, Daseking M, Jacobs C, et al.

The Wechsler Scales have been proven effective in identifying specific cognitive deficits that are associated with different psychiatric disorders. With its new test structure, the German version of the recent Wechsler Intelligence Scale for Children Fifth Edition (WISC-V; Wechsler, 2017) enables amore in-depth examination

of intellectual abilities. The present study focused on the nature of cognitive deficits in ADHD. The aim was to analyze the performances of 103 children and adolescents with ADHD on the WISC-V and to compare them with a matched control group. Analyses of variances were conducted and group differences were examined by means of effect sizes (Cohen's d) in order to demonstrate possible cognitive deficits associated with ADHD. The results of the present study revealed significantly lower performances of children with ADHD when compared with healthy controls. On the index level, effect sizes ranged from d = 0.29 for Verbal Comprehension to d = 0.74 for Working Memory. In line with the literature, significant deficits of children with ADHD in Processing Speed were also supported by the present findings (d = 0.45). Despite some contrary findings from previous studies, a significantly lower mean FSIQ score could be identified for the clinical group, with a medium effect size of d = 0.67. WISC-V profiles additionally disclosed the diversity of cognitive deficits related to the disorder. Since the largest effects could be shown for Digit Span (d = 0.89), Letter Number Sequencing (d = 0.67), and Arithmetic (d = 0.62), these WISC-V subtests can be considered to be sensitive to cognitive declines in ADHD. Despite the fact that the mean index and FSIQ scores of children with ADHD were all within one standard deviation below the population mean, about one third of these children fulfilled the criteria for borderline intellectual functioning in the present study. Given that disorder-related deficits could be demonstrated in Visual-Spatial as well as in Fluid Reasoning, the WISC-V can be considered suitable for detecting executive dysfunctions in ADHD. Since at least some cognitive deficits in ADHD were found to be more pronounced than expected, the role of the severity of symptoms and further possible contributing factors are finally discussed. Although the current results support the assumption that ADHD is associated with deficits in Working Memory, Fluid Reasoning, and Processing Speed, there are some study limitations to be addressed. Since previous studies highlighted the effects of further factors contributing to cognitive deficits in ADHD, it is recommended for future studies to take possible effects of comorbid disorders and severity of the disorder into consideration when analyzing cognitive profiles in ADHD. In clinical practice, the WISC-V profiles can provide additional information for decision-making but should not be used alone to carry out a clinical diagnosis

Minerva Pediatr. 2018:70:355-59.

EVALUATION OF COMBINED EFFECTS OF BRAIN ELECTRONIC BIOFEEDBACK TRAINING AND PSYCHO-BEHAVIOR INTERVENTION IN ADHD AFFECTED CHILDREN.

Chen J, Liu X, Zhang D.

**BACKGROUND**: The present study aimed to explore the potential effects of brain electronic biofeedback training in combination with psycho-behavior intervention during non-medical treatment of children with attention deficit hyperactivity disorder (ADHD).

**METHODS**: The children with ADHD admitted to our department from January 2015 to January 2016 were selected as the study subjects. All the cases met the standard of Chinese classification of mental disorders criterion and were divided into two groups, the control group and the observation group, with 15 cases in each group. Medical treatment and brain electronic biofeedback training were provided for the children in the control group; while medical treatment and brain electronic biofeedback training in combination with psychobehavior intervention were provided to children in the observation group. For both groups, one course lasted for three months, after which questionnaires were distribute in order to evaluate the application effects.

**RESULTS**: The symptoms of the children in the two groups were improved after the treatment. However, the improvement in observation group was significantly higher that of the children in the control group.

**CONCLUSIONS**: Brain electronic biofeedback training in combination with psycho-behavior intervention is significantly better treatment option for children affected with ADHD

Mol Psychiatry. 2018;1-19.

TREATMENT STRATEGIES FOR ADHD: AN EVIDENCE-BASED GUIDE TO SELECT OPTIMAL TREATMENT.

## Caye A, Swanson JM, Coghill D, et al.

Attention-deficit/hyperactivity disorder (ADHD) is a common and impairing disorder affecting children, adolescents, and adults. Several treatment strategies are available that can successfully ameliorate symptoms, ranging from pharmacological to dietary interventions. Due to the increasing range of available options, an informed selection or prioritization of treatments is becoming harder for clinicians. This review aims to provide an evidence-based appraisal of the literature on ADHD treatment, supplemented by expert opinion on plausibility. We outline proposed mechanisms of action of established pharmacologic and non-pharmacologic treatments, and we review targets of novel treatments. The most relevant evidence supporting efficacy and safety of each treatment strategy is discussed. We review the individualized features of the patient that should guide the selection of treatments in a shared decision-making continuum. We provide guidance for optimizing initiation of treatment and follow-up of patients in clinical settings

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Neuro Endocrinol Lett. 2018 Feb;38:549-54.

QTC PROLONGATION AFTER ADHD MEDICATION.

Snircova E, Marcincakova H, V, Ondrejka I, et al.

**OBJECTIVE**: Multicenter studies have shown that cardiovascular risks of ADHD medication are extremely low. However, QTc length has been shown to be increased in smaller samples of patients or case reports after stimulant and atomoxetine medication. Based on recent studies of genetic polymorphisms associated with drug-induced QTc prolongation and polymorphisms linkage to regional populations, we hypothesized that the drug-induced QTc prolongation could be a factor of particular polymorphisms linked to specific regional populations undistinguished in multicenter studies.

**METHODS**: We included 69 patients from a region of central Slovakia, 36 patients were taking atomoxetine and 33 patients methylphenidate. QTc, heart rate, potassium levels and BMI were examined before and after 8 weeks of treatment. Therapeutic effect was measured by ADHD-RS-IV.

**RESULTS**: We found QTc prolongation after 8 weeks of treatment both with atomoxetine and methylphenidate that was neither followed by the significant changes in BMI and potassium levels nor the significant increase of heart rate.

**CONCLUSION**: This is the first study revealing QTc prolongation in the group of ADHD children from the same region after 8-week treatment with atomoxetine and methylphenidate, indicating the potential discrete abnormalities in cardiac functioning associated with polymorphisms in genes of dopaminergic and noradrenergic system

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Neurol Psychiatry Brain Res. 2018;29:22.

FOOD INTOLERANCE AND ADHD.

Schneider-Momm K, Kaiser I, Overdick L, et al.

**Introduction**: A potential correlation between hyperactivity and food has already been described in the beginning of the last century. The systematic review and meta-analysis of Sonuga-Barke (2013) summarizes all non-pharmacological treatments of ADHD, including the oligoantigenic diet. Referring to the INCA study of Pelsser (2011) our study investigates the influence of dietary regimes on symptoms of children suffering ADHD, with the objective of evaluating individual food recommendation as a therapeutic approach in ADHD treatment.

**Methods**: The study includes 24 children between 7 and 18 years with the diagnosis of ADHD without stimulant medication and is performed in an ambulatory setting. Our study protocol takes four weeks of strict food elimination, followed by a food reintroduction phase with personal food recommendations. The children's behavior is assessed with the ADHD-Rating-Scale (parent report inventory). Responders with a change of behavior of at least 40% after the diet continue the study phase.

**Results**: 14 of 24 patients showed improvement upon dietary treatment with values between 27 and 82% on the ADHD-Rating-Scale. The mean outcome of improvement of Responders is 51%. The follow-up showed a further fall on the ARS upon strict food recommendations.

**Conclusion**: Our study suggests, that restricted elimination diet reduces symptoms in children suffering ADHD and that individual food recommendations should be a valid therapeutic approach

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Neuropsychiatr Dis Treat. 2018;14:1671-83.

CLINICIAN-DELIVERED COGNITIVE TRAINING FOR CHILDREN WITH ATTENTION PROBLEMS: EFFECTS ON COGNITION AND BEHAVIOR FROM THE THINKRX RANDOMIZED CONTROLLED TRIAL.

## Moore AL, Carpenter DM, Miller TM, et al.

**Purpose**: The impact of attention problems on academic and social functioning coupled with the large number of children failing to respond to stimulant medication or behavioral therapy makes adjunctive therapies such as cognitive training appealing for families and clinicians of children with attention difficulties or childhood attention deficit hyperactivity disorder. However, the results of cognitive training studies have failed to find far transfer effects with this population. This study examined the quantitative cognitive effects and parent-reported behavioral effects of a clinician-delivered cognitive training program with children who have attention problems.

Patients and methods: Using a randomized controlled study design, we examined the impact of a clinician-delivered cognitive training program on processing speed, fluid reasoning, memory, visual processing, auditory processing, attention, overall intelligence quotient score, and behavior of students (n=13) aged 8-14 years with attention problems. Participants were randomly assigned to either a waitlist control group or a treatment group for 60 hours of cognitive training with ThinkRx, a clinician-delivered intervention that targets multiple cognitive skills with game-like, but rigorous mental tasks in 60-90-minute training sessions at least 3 days per week.

**Results**: Results included greater mean pretest to posttest change scores on all variables for the treatment group versus the control group with statistically significant differences noted in working memory, long-term memory, logic and reasoning, auditory processing, and intelligence quotient score. Qualitative outcomes included parent-reported changes in confidence, cooperation, and self-discipline.

**Conclusion**: Children with attention problems who completed 60 hours of clinician-delivered ThinkRx cognitive training realized both cognitive and behavioral improvements

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Neurorehabilitation and Neural Repair. 2018;32:373.

META-COGNITION IN CHILDREN WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER AN OCCUPATIONAL THERAPY COHORT STUDY.

## Iyer AS, Nandgaonkar H.

**Objectives**: ADHD is also considered as a disorder of executive functions. (Russell Barkley PhD). The objective of this study is to understand the role of occupational therapy in managing meta cognitive functions in children with ADHD

**Methods**: 10 children with ADHD in the age range 6-10 years participated in the study. They were assessed on Sensory Profile Caregiver Questionnaire (SPCQ). Individualized goals were set for each child using Goal Attainment Scaling (GAS). Occupational therapy program targeting meta cognitive skills/executive functions was provided for 12 weeks. Alert Program -® was also used as an adjunct.

**Results**: 1) SPCQ shows significant improvement as per paired t test (P < 0.05) in sub sections post intervention. The percentage changes being Sensory Processing (4.5%), Modulation (9.2%), Behavior & Emotional Responses (7.9%). SPCQ ADHD worksheet also showed changes post intervention. 2) As per GAS 20% less than expected outcomes, 54% expected outcomes and 22% more than expected outcomes achieved post intervention.

**Conclusions**: This study, gave an insight into the role of the comprehensive occupational therapy program in facilitating better meta cognitive/ executive functions in children with ADHD which was seen in the form of

decreased inattention/distractibility, improved on-task behaviors and improved social behaviors at home and school

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Nutrients. 2018;10.

PSYCHIATRIC COMORBIDITY IN CHILDREN AND ADULTS WITH GLUTEN-RELATED DISORDERS: A NARRATIVE REVIEW . Slim M, Rico-Villademoros F, Calandre EP.

Gluten-related disorders are characterized by both intestinal and extraintestinal manifestations. Previous studies have suggested an association between gluten-related disorder and psychiatric comorbidities. The objective of our current review is to provide a comprehensive review of this association in children and adults. A systematic literature search using MEDLINE, Embase and PsycINFO from inception to 2018 using terms of celiac disease or gluten-sensitivity-related disorders combined with terms of mental disorders was conducted. A total of 47 articles were included in our review, of which 28 studies were conducted in adults, 11 studies in children and eight studies included both children and adults. The majority of studies were conducted in celiac disease, two studies in non-celiac gluten sensitivity and none in wheat allergy. Enough evidence is currently available supporting the association of celiac disease with depression and, to a lesser extent, with eating disorders. Further investigation is warranted to evaluate the association suggested with other psychiatric disorders. In conclusion, routine surveillance of potential psychiatric manifestations in children and adults with gluten-related disorders should be carried out by the attending physician

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Paediatrics and Child Health (Canada). 2018;23:e35.

PARENTAL PERCEPTIONS OF MEDICATION IMPACT ON BEHAVIOUR AND LEARNING IN CHILDREN WITH ATTENTION/DEFICIT-HYPERACTIVITY DISORDER.

Lemay J-F, Lemay J-A, Kubas H.

**BACKGROUND**: Attention-deficit/hyperactivity disorder (ADHD) is a neurodevelopmental disorder that often negatively impacts behaviour, cognition, and learning. Stimulant medications are the most commonly used treatment for ADHD, with informant reports (e.g., parent questionnaires, surveys) frequently used to evaluate medication impact on behavioural and academic functioning in affected children.

**OBJECTIVES**: To determine parental perceptions of medication impact on behaviour and learning in a long-acting methylphenidate (LA-MPH) trial of their children with ADHD.

**DESIGN/METHODS**: A randomized controlled LA-MPH medication trial was conducted with children ages 8-12 with a diagnosis of ADHD. Trial began with one-week of baseline assessment, followed by a randomized three-week standard of care medication trial, and a one-week best dose assessment. Following the conclusion of the study (6 months to 2 years' range post-treatment), families were asked to participate in a voluntary follow-up phone survey to evaluate parental perceptions on child's behaviour and learning. RESULTS: A total of 34/42 (81%) families participated (male to female ratio: 2.1/1). At the time of the follow-up survey, 53% (18/34) and 68% (23/34) of patients were having difficulty or significant difficulty with their behaviour and learning, respectively. Twenty-three patients (68%) were still on psycho-stimulant medications. Although parents of those 23 children said LA-MPH had in general significant or very significant impact on their child's behaviour (87%) and learning (79%), these parents were still reporting challenges with behaviour (52%) and learning (61%) at follow-up. In addition, parents of children not on medication said that their current child's behaviour and learning was still having the same or more challenging issues (82% and 73% respectively).

**CONCLUSION**: Overall, parents reported that medication significantly impacted their child's behaviour and learning however, long-term medication impact appears less effective. Thus, an ongoing relationship with families and paediatricians is recommended to better understand the impact of medication on behaviour and learning. Evaluating the effects of medication on behaviour and learning may ultimately lead to targeted intervention that help foster long-term treatment efficacy for children with ADHD

Paediatrics and Child Health (Canada). 2018;23:e34.

EVALUATION OF EXECUTIVE FUNCTIONING AND BEHAVIOUR IN YOUNG ADOLESCENTS WITH ADHD: A FOLLOW-UP STUDY.

Lemay J-F, Hai T, Kubas H, et al.

**BACKGROUND**: Executive functioning (EF) impairment is frequent in the ADHD population. Psychostimulant medications (e.g. Methylphenidate [MPH]) are considered effective in reducing EF symptomatology. Limited studies have investigated the long-term effects of MPH on EF in young adolescents with ADHD (A-ADHD).

**OBJECTIVES**: To evaluate EF and behaviour challenges across three time points in A-ADHD who were involved in a MPH treatment trial. EF and behavioural functioning were evaluated using two separate parent questionnaires.

**DESIGN/METHODS**: A total of 21 A-ADHD (males=62% n=13), ages 9-14 (M=12.33 years, SD=1.55 years) were evaluated at three separate time points: 1) Baseline (BL: no medication) 2) Best Dose (BD: following a 4-week trial of MPH treatment) and 3) long term Follow-Up (FU: defined as up to 2 years following best dose). Parents completed two behaviour rating scales: Behaviour Rating Inventory of Executive Functioning (BRIEF) and Behaviour Assessment System for Children (BASC-2). Repeated measures analyses of variance (RmANOVA) were conducted measuring changes in EF and behavioural challenges over the three time points (BL, BD, and FU).

**RESULTS**: Significant differences were obtained in EF ratings over time on the BRIEF Behavioural Regulation Index (BRIEF-BRI F (2,36) = 20.71, p < 0.001) and Metacognition Index (BRIEF-MI F (2,36) = 26.83, p < 0.001). Pairwise comparison indicated a) significant decrease in symptom ratings for both indexes between time points BL and BD, and b) significant increase in symptom ratings for indexes between time points BD and FU. Similarly, behavioural ratings obtained on all BASC-2 indexes (Externalizing Problems, Internalizing Problems, Behavioral Symptoms, and Adaptive Skills) revealed a significant effect of time (F (2,36) range = 4.55 to 26.28, p range = <.001 to <.05). Pairwise comparison indicated a) significant decrease in symptom ratings across all BASC-2 indexes between BL and BD, and b) increase in symptom ratings across all BASC-2 indexes between BD and FU time points. Therefore, parent ratings indicated clinically significant difficulties with EF and behaviour during BL and FU and average EF and behaviour scores during BD.

**CONCLUSION**: During follow-up, parents of A-ADHD continue to report challenges in EF and in all aspects of behaviours and adaptive skills. Although parents reported positive changes during the MPH trial (BD), these behavioural improvements were not seen at follow-up. The combined use of screening tools for EF (BRIEF) and behaviour (BASC-2) might be of interest to paediatricians when monitoring medication responses in young adolescents with ADHD

Paediatrics and Child Health (Canada). 2018;23:e6.

ATTENTION-DEFICIT/HYPERACTIVITY DISORDER (ADHD) IN SCHOOL-AGED CHILDREN AT TWO SCHOOL BASED HEALTH CENTERS (SBHCS): A DESCRIPTIVE STUDY.

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Ghosh N, Aiyadurai R, Freeman S.

**BACKGROUND**: The number of school-aged children diagnosed with ADHD in Canada has been on the rise over the past three decades. Evidence suggests that children with ADHD dealing with risk factors, such as poverty and prolonged wait-times are more likely to have poorer outcomes due to challenges in accessing healthcare services. Schools are ideal for the early identification of children with ADHD, as they are often the setting in which attention and behavioural issues come to light. School-Based Health Centres (SBHCs) are embedded within the school system and are an ideal entry point for children with ADHD into the healthcare system.

**OBJECTIVES**: To examine the prevalence of ADHD and as well as demographic characteristics and time to assessment of children at two inner-city SBHCs in Toronto.

**DESIGN/METHODS**: A retrospective chart review was performed on 869 children from November 2010-March 2016 from two SBHCs. Frequency measures were used to determine the proportion of children that received a new diagnosis of ADHD. Within this population, the patient's age, gender, ethnicity, parental income, home arrangement, parental education and newcomer status were described. Diagnostic waittimes

within the SBHC were calculated using two specific data points -a child's first clinic visit data and the clinic date they saw a general paediatrician, who would provide the ADHD diagnosis.

**RESULTS**: Of the 869 children, 9.6% of children received a new diagnosis of ADHD. The mean age of diagnosis was 7.6 years and 80% of the children were male. 74.6% of children's families identified them as an ethnicity other than white. 60.2% of the patients' household income was <\$30,000/year. 44.5% of the families were composed of single-parent households. 52.8% of the patients' mothers and 47.6% of fathers had completed a high school level of education or less. 34% of the children were not born in Canada, and of those, 57% had been in the country for only 0-3 years. The average wait time for a child to see a general paediatrician for a developmental assessment from initial visit date was 62.3 days.

**CONCLUSION**: The prevalence of ADHD at 2 SBHCs was higher than that reported in the general population. A number of barriers to health care access were identified in this cohort of children including low income, single parent homes and newcomer status. SBHCs serve as an accessible health care model that can provide timely diagnosis and management to vulnerable children with ADHD which may improve outcomes

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Pediatr Dermatol. 2016;33:690-91.

FEW ATOPIC DERMATITIS CHILDREN WITH SLEEP DISTURBANCE MEET VANDERBILT CRITERIA FOR ADHD.

## Kruse L, Boor P, Cices A, et al.

**Introduction**: Epidemiological studies have uncovered an association between attention deficit hyperactivity disorder (ADHD) and atopic dermatitis (AD) and other atopic disorders in children. Sleep is disrupted in up to 60% of children with AD and in 83% during disease exacerbations. Chronic sleep disturbance can have deleterious effects on neurocognitive function and school performance.

**Objective**: To determine if sleep disturbance is associated with the severity of AD, and explore the relationships between ADHD, sleep disturbance and AD. Our hypothesis was that children with more severe AD have increased sleep disruption, resulting in poor neurocognitive function and restlessness, which could meet criteria for ADHD.

**Methods**: Children ages 6-17 years (n = 15) with moderate to severe AD (Scoring AD [SCORAD] >25) were recruited from dermatology and allergy clinics. Sleep disturbance was assessed via nighttime actigraphy (Actiwatch Spectrum) with 30s epoch length, measured for 7 consecutive nights. Sleep questionnaires were concurrently administered during this 7 night period. Subjective pruritus was assessed via Visual Analogue Scale (VAS) and neurocognitive function was evaluated with standardized Vanderbilt assessments completed by a parent and teacher for ADD/ADHD.

**Results**: Only 2 of the 15 children (1 male and 1 female) were found to have ADD/ADHD via parent-completed Vanderbilt forms. Sleep disturbance as judged by minutes of being awake after sleep onset (WASO) was correlated with AD severity (r = 0.61, p = 0.02). However, sleep disturbance (WASO or awakenings) did not correlate with higher inattention symptoms scores (ISS) (r = 0.14, p = 0.62 and r = 0.15, p = 0.60). Moreover, AD severity did not correlate with ISS (r = 0.08, p = 0.78) and the average ISS was the similar in children categorized with moderate (SCORAD 25-50) vs. severe AD (SCORAD >50) at 11.8 3.6 (SE) v. 14.9 5.3 (p = 0.7).

**Discussion**: Patients with severe AD are more likely to experience sleep disturbance. However, in our small cohort, these sleep disturbances did not translate into higher inattention scores. Our cohort had a screening prevalence of ADHD similar to the general population, despite moderate to severe AD and sleep disturbance. Future work to determine the relationship between sleep disturbance and neurocognitive function in children with AD should consider multi-center recruitment to achieve sufficient numbers of children with ADHD and evaluation of other types of neurocognitive function

Pediatric Radiology. 2018;1-9.

RADIOGRAPHIC APPEARANCE AND CLINICAL SIGNIFICANCE OF FIDGET SPINNER INGESTIONS.

Sammer MBK, Kan JH, Sammer MD, et al.

**Background**: According to anecdotal press reports, there have been medically significant ingestions of fidget spinner toys, including ingestions that required endoscopic intervention. Fidget spinners have been marketed to improve attention and have been suggested as a therapeutic alternative to medications in children with attention deficit hyperactivity disorder (ADHD).

**Objective**: To describe the radiographic appearance and features of ingested fidget spinner components. To evaluate clinical significance via rates of endoscopic intervention, incidence in patients on ADHD medications, and mean age compared to other accidental foreign body ingestions.

**Materials and methods**: A nested retrospective case control study analyzed pediatric accidental foreign body ingestions identified via electronic medical record search between March 1, 2017, and Feb. 28, 2018. Radiographic identifiability, component type and maximum diameter of ingested fidget spinner components were described. A nested cohort of non-fidget spinner ingestions between May 1 and Aug. 31, 2017, was compared with the fidget spinner ingestions for rates of endoscopic intervention (a), concomitant use of ADHD medication (b) and mean age (c) using the Fisher exact test (a and b) and independent samples t-test (c).

**Results**: There were 1,095 unintentional foreign body ingestions. Ten were ingested fidget spinner component ingestions. Eight of the 10 ingested components were radiographically identifiable. Compared with the nested cohort of non-fidget spinner ingestions, fidget spinner ingestions were more likely to undergo endoscopic intervention (P=0.009, 5/10 fidget spinner ingestions vs. 54/383 other ingestions). Fidget spinner patients were more likely to be on ADHD medication (P=0.011, 2/10 fidget spinners vs. 5/383 other). Fidget spinner mean patient age was significantly older than other ingestions (P=0.015, mean: 7.1 years fidget spinner ingestions vs. 4.0 years for other ingestions).

**Conclusion**: Compared with other foreign body ingestions, patients who ingested fidget spinner components were more likely to undergo endoscopic intervention, had a higher rate of ADHD medication use and were older. Familiarity with the radiographic appearance of ingested fidget spinner components is important for patient management

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Pediatr Int. 2018:60:529-34.

INTERNET ADDICTION AND ATTENTION-DEFICIT \( \bar{\cupec}\) OHYPERACTIVITY DISORDER: \( \bar{\cupec}\) FFECTS OF ANXIETY, DEPRESSION AND SELF-ESTEEM.

### Kahraman, Demirci E.

**Background**: Attention-deficit hyperactivity disorder (ADHD) is one of the most common neurodevelopmental disorders of childhood. Behavioral disinhibition, poor neurocognitive skills and immediate reward preference in children with ADHD have been suggested as risk factors for Internet addiction (IA). The aim of the present study was therefore to investigate the relationship between IA and depression, anxiety, and self-esteem in adolescents with ADHD, and to identify the features of Internet use that predict IA.

**Methods**: We studied 111 patients with ADHD aged 12-18-years, and 108 healthy controls. The ADHD patients and controls were asked to complete a sociodemographic data form, the Internet Addiction Scale (IAS), Children's Depression Inventory, Childhood Screening Scale for Anxiety in Children, and the Rosenberg Self-Esteem Scale.

**Results**: IAS total score in the adolescents with ADHD was significantly higher than in the control group. Compared with the control group, the ADHD group depression scale score was significantly higher, and self-esteem score significantly lower (P < 0.05 for both). There was no difference between the groups in anxiety score. IAS score had a positive correlation with depression and anxiety scores, and a negative correlation with self-esteem score.

**Conclusion**: The relationship between IA scale score and depression, anxiety and self-esteem scale scores were similar in the ADHD and the control group. In addition, IAS subscale and total scores were significantly higher in the ADHD group than the control group, even after controlling for the effects of self-esteem,

depression and anxiety scores. Thus, ADHD is thought to be an independent risk factor for depression, anxiety and self-esteem, and, hence, for IA

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PLoS ONE. 2018;13.

OUTPATIENT REHABILITATION RESOURCES AND MEDICAL EXPENDITURE IN CHILDREN WITH ATTENTION-DEFICIT HYPERACTIVITY DISORDER IN TAIWAN.

### Li H-J, Kuo C-C, Yao Y-C, et al.

Attention-deficit hyperactivity disorder (ADHD) is a neurodevelopmental disorder in children. This study investigated the use of rehabilitation treatment in Taiwan. We selected children aged 3-12 years from the National Health Insurance Research Database from 2008 to 2012 and included them in the analysis. The children who received a diagnosis according to the International Classification of Diseases, Ninth Revision, Clinical Modification were divided into two groups: ADHD and non-ADHD. We used the chi-squared test, independent sample t test, and multiple regression analysis to conduct the analysis. The utilisation of rehabilitation resources was higher in the ADHD group than in the non-ADHD group. The number of schoolaged children with ADHD was higher than the number of preschool-aged children (p < 0.001). The highest utilisation of rehabilitation resources was observed in clinics (p < 0.001). In terms of region, Taipei exhibited the highest utilisation of rehabilitation resources, and the East exhibited the lowest resource utilisation (p < 0.001). Prediction of the use of rehabilitation resources, average cost, average frequency of visits, and total annual cost was affected by factors such as the average frequency of rehabilitation use, demographic characteristics, and the hospital characteristics and location (p < 0.001). The number of children with ADHD and rehabilitation use are increasing yearly; however, limitations in payment restrict the growth of rehabilitation resource use in hospitals. Supplementation of rehabilitation resources at clinics accounts for more than 60%, however, the total annual cost is less than what is observed for hospitals (p < 0.001). Policies should be established to aid in the early detection and treatment of children with ADHD to improve treatment outcomes and reduce the family burden and treatment expenditure in the future

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PLoS ONE. 2018;13:e0194856.

A GENERAL PREDICTION MODEL FOR THE DETECTION OF ADHD AND AUTISM USING STRUCTURAL AND FUNCTIONAL MRI.

### Sen B, Borle NC, Greiner R, et al.

This work presents a novel method for learning a model that can diagnose Attention Deficit Hyperactivity Disorder (ADHD), as well as Autism, using structural texture and functional connectivity features obtained from 3-dimensional structural magnetic resonance imaging (MRI) and 4-dimensional resting-state functional magnetic resonance imaging (fMRI) scans of subjects. We explore a series of three learners: (1) The LeFMS learner first extracts features from the structural MRI images using the texture-based filters produced by a sparse autoencoder. These filters are then convolved with the original MRI image using an unsupervised convolutional network. The resulting features are used as input to a linear support vector machine (SVM) classifier. (2) The LeFMF learner produces a diagnostic model by first computing spatial non-stationary independent components of the fMRI scans, which it uses to decompose each subject's fMRI scan into the time courses of these common spatial components. These features can then be used with a learner by themselves or in combination with other features to produce the model. Regardless of which approach is used, the final set of features are input to a linear support vector machine (SVM) classifier. (3) Finally, the overall LeFMSF learner uses the combined features obtained from the two feature extraction processes in (1) and (2) above as input to an SVM classifier, achieving an accuracy of 0.673 on the ADHD-200 holdout data and 0.643 on the ABIDE holdout data. Both of these results, obtained with the same LeFMSF framework, are the best known, over all hold-out accuracies on these datasets when only using imaging data-exceeding previously-published results by 0.012 for ADHD and 0.042 for Autism. Our results show that combining multimodal features can yield good classification accuracy for diagnosis of ADHD and Autism, which is an important step towards computer-aided diagnosis of these psychiatric diseases and perhaps others as well

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Scand J Public Health. 2018 Mar;46:262-71.

SUBJECTIVE HEALTH COMPLAINTS AND EXPOSURE TO PEER VICTIMIZATION AMONG DISABLED AND NON-DISABLED ADOLESCENTS: A POPULATION-BASED STUDY IN SWEDEN.

Fridh M, Kohler M, Moden B, et al.

**AIMS**: To investigate subjective health complaints (SHCs) (psychological and somatic, respectively) among disabled and non-disabled adolescents, focusing on the impact of traditional bullying and cyber harassment, and furthermore to report psychological and somatic SHCs across different types of disability.

**METHODS**: Data from the public health survey of children and adolescents in Scania, Sweden, 2012 was used. A questionnaire was answered anonymously in school by 9791 students in the 9th grade (response rate 83%), and 7533 of these with valid answers on key questions were included in this study. Associations with daily SHCs were investigated by multi-adjusted logistic regression analyses.

**RESULTS**: Any disability was reported by 24.1% of boys and 22.0% of girls. Disabled students were more exposed to cyber harassment (boys: 20.0%; girls: 28.2%) than non-disabled peers (boys: 11.8%; girls: 18.1%). Exposure to traditional bullying showed the same pattern but with a lower prevalence. Disabled students had around doubled odds of both daily psychological SHCs and daily somatic SHCs in the fully adjusted models. In general, the odds increased with exposure to cyber harassment or traditional bullying and the highest odds were seen among disabled students exposed to both cyber harassment and traditional bullying. Students with ADHD/ADD had the highest odds of daily psychological SHCs as well as exposure to traditional bullying across six disability types.

**CONCLUSIONS**: Disabled adolescents report poorer health and are more exposed to both traditional bullying and cyber harassment. This public health issue needs more attention in schools and in society in general

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Sports Health. 2018 Jul;10:317-26.

NEUROCOGNITIVE DEFICITS ASSOCIATED WITH ADHD IN ATHLETES: A SYSTEMATIC REVIEW.

Poysophon P, Rao AL.

**CONTEXT**: Attention deficit hyperactivity disorder (ADHD) is a common childhood disorder and is frequently diagnosed in young adults. Emerging studies suggest a relationship between ADHD and concussion. **OBJECTIVE**: To determine whether athletes with ADHD are at increased risk for neurocognitive deficits related to concussion risk, symptom reporting, and recovery.

**DATA SOURCES**: A comprehensive search of PubMed, CINAHL, PsychInfo, and Cochrane Library databases was performed. Studies conducted between 2006 and 2017 were reviewed, although only those between 2013 and 2017 met inclusion criteria.

**STUDY SELECTION**: Studies that examined neurocognitive deficits in adolescent and young adult athletes aged 15 to 19 years who had ADHD and reported using notable neuropsychological evaluation tools were included.

**STUDY DESIGN**: Systematic review.

LEVEL OF EVIDENCE: Level 2.

**RESULTS**: A total of 17 studies met the inclusion criteria. The prevalence of ADHD in athletes varied between 4.2% and 8.1%. Overall, athletes with ADHD demonstrated lower scores on neurocognitive testing such as the ImPACT (Immediate Post-Concussion Assessment and Cognitive Test), increased risk for concussion, and increased symptom reporting. There was no evidence that treatment with stimulant medication changed these risks.

**CONCLUSION**: ADHD is associated with increased neurocognitive deficits in athletes, although pathophysiology remains unclear. Evidence for stimulant treatment in athletes with ADHD continues to be sparse

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The Clinical Neuropsychologist. 2018 Jul;32:783-815.

PROSPECTIVE MEMORY IN CHILDREN WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER: A REVIEW.

#### Talbot KD, et al.

**Objective**: The objective of the paper is to synthesize the research on prospective memory (PM) in children with attention-deficit/hyperactivity disorder (ADHD).

**Method**: Research on PM and ADHD in youth was synthesized according to the PRISMA guidelines and a summary of the types of PM deficits typically seen in these children, as well as the methods currently available to assess and treat these deficits is provided. Suggestions on ways to better manage PM deficits in children's everyday lives are also discussed.

**Results**: Six studies have investigated PM in children with ADHD. The majority of these studies found a deficit in time-based PM, but not event-based PM. The mechanisms underlying this deficit, however, are still unknown. There are currently no specific measures available to clinically assess PM in children and there are no specific evidence-based interventions available that specifically target PM deficits in children with ADHD.

**Conclusion**: Remediation strategies aimed at compensating for these PM deficits in daily life may be most useful. Nevertheless, more research is necessary to better understand PM in children with ADHD

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Z Kinder- Jugendpsychiatr Psychother. 2018;46:285-97.

THE INTERPARENTAL RELATIONSHIP IN FAMILIES WITH CHILDREN WITH ADHD: INTERACTIONS BETWEEN COUPLE DISTRESS AND CHILD'S SYMPTOMS.

### Zemp M.

The impact of the family in the development and maintenance of childhood ADHD is well established. However, previous research in this fi eld focused largely on parenting and the quality of the parent-child relationship, whereas the role of the interparental relationship has been neglected. This review summarizes the current state of research on the interactions between a couple distress and their child's ADHD and discusses interparental conflict as a risk factor for the development of ADHS-related symptoms. Based on the present knowledge, an integrative model is postulated that assumes an interaction of genetic vulnerability for childhood ADHD and a couple distress. It depicts how distress in the interparental relationship may both directly and indirectly affect the etiology, maintenance, and/or amplifi cation of childhood ADHD-related symptoms, which in turn affect the interparental relationship. The review highlights the signifi cance of relationship distress prevention programs for couples to prevent adjustment problems in children, and the adequate consideration of couple conflict in diagnostics and therapy among families with children with ADHD

Zhonghua Liu Xing Bing Xue Za Zhi. 2018 Apr;39:464-68.

POTENTIAL INTERACTION EFFECT ON ATTENTION-DEFICIT/HYPERACTIVITY DISORDER BETWEEN MOTHER'S EDUCATIONAL LEVEL AND PRESCHOOLERS' DIETARY PATTERN.

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**Objective**: To explore the interaction effect between mother's educational level and preschoolers' dietary pattern on attention-deficit/hyperactivity disorder (ADHD).

**Methods**: In 2014, there were 16 439 children aged 3-6 years old from 91 kindergartens in Ma'anshan municipality of China. A semi-quantitative food frequency questionnaire and the 10-item Chinese version of the Conners' Abbreviated Symptom Questionnaire (C-ASQ) were administered to assess the usual dietary intake and symptoms on ADHD. Social-demographic information was collected through questionnaires.

Unconditional logistic regression was used to analyze the multiplication interaction effect between mother's educational level and preschoolers' dietary pattern on ADHD. Excel software was used to analyze the additive interaction effect of mother's educational level and preschoolers' dietary pattern on ADHD.

**Results**: Results showed that factors as: mother's low educational level[aOR=1.31 (1.13-1.52)], scores related to preschoolers in the top quintile of "food processing" [aOR=1.31 (1.16-1.48)] and "snack" [aOR=1.45 (1.29-1.63)] patterns showed greater odds while preschoolers in the top quintile of "vegetarian" [aOR=0.80 (0.71-0.90)]showed less odds for having ADHD symptoms. Both multiplication and additive interactions were observed between mothers with less education. The processed dietary patterns (OR=1.17, 95%CI: 1.11-1.25), relative excess risk of interaction (RERI), attributable proportion (AP) and the interaction index (SI) appeared as 0.21, 0.13 and 1.47, respectively. Multiplication interaction was observed between levels of mother's low education and the snack dietary pattern (OR=1.21, 95%CI: 1.14-1.29), with RERI, AP and SI as 0.49, 0.26 and 2.36, respectively. However, neither multiplication interaction or additive interaction was noticed between levels of mother's low education and the vegetarian dietary pattern (OR=0.97, 95%CI: 0.92-1.03), with RERI, AP and SI as 0.09, 0.05 and 1.15, respectively.

**Conclusions**: Levels of mother's low education presented a risk factor for ADHD symptoms in preschool children. Both multiplication interaction and additive interaction were observed between mother's low education levels and the processed dietary pattern. Multiplication interaction was noticed between mother's education levels and the snack dietary pattern but not with the vegetarian dietary pattern

#### PW0666

# Bipolar disorder in ADHD: frequent comorbidity or severe neurodevelopmental disorder?

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*Background.*– The aim of the present study was to evaluate prevalence and clinical variables of patients with and without bipolar disorder in a sample of adult ADHD outpatients.

Methods.— We examined all medical records of outpatients accessing the adult ADHD center of the AOU San Luigi Gonzaga, Orbassano (TO), Italy, in order to collect data about socio-demographic factors, medical history, medical and psychiatric diagnosis. Adult DSM-IV ADHD diagnosis was made by DIVA 2.0 whereas DSM-IV comorbidities were assessed by SCID I and II.

Results.— Above one quarter of our sample with ADHD (26,6%) had also a bipolar disorder that was a type II in almost all of cases (90,5%). ADHD combined type (ADHD-C) is more common than inattentive type (ADHD-I) in patients with bipolar disorder only (ADHD+DB; ADHD-C:85,7% vs. ADHD-I:14.3%; ADHD; ADHD-C:51,7% vs. ADHD-I:48,3%; p=0,006). ADHD-C is more common in bipolar patients even in childhood (ADHD+DB; ADHD-C:65% vs. ADHD-I:25% vs. ADHD-H:10%; ADHD; ADHD-C:52% vs. ADHD-I:48%; P=0.048).

Moreover, ADHD with bipolar disorder had more frequently a comorbid psychiatric disorder or other co-occurring conditions (personality disorder, 19% vs. 1,8%, P=0.006; sleep disorder, 52.3% vs. 32.7%, P=0.009; use of benzodiazepines without anxiety disorder, 47.6% vs. 10.9%, P=0.001; immune system disease, 23.8% vs. 5.2%, P=0.015).

Conclusions.— Our findings are consistent with previous studies reporting a high prevalence of bipolar II disorder among adults with ADHD. ADHD patients with comorbid bipolar disorder seem most likely to have shown a combined manifestation of inattention and hyperactivity in childhood that evolved in a complex and severe clinical picture with personality and sleep disorders comorbidities. Disclosure of interest.— The authors have not supplied a conflict of interest statement.

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## CS0013

## **Epidemiology of ADHD and SUD**

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Attention-deficit/hyperactivity disorder (ADHD) has been primarily considered, for a long time, a childhood condition. Despite it, recent data suggest that symptoms of ADHD continue into adulthood in up to 50% of people diagnosed as affected by ADHD during their childhood. Accurate diagnosis of ADHD in adults is challenging and requires attention to early development and symptoms of inattention, distractibility, impulsivity and emotional liability. Currently, it does not exist a "gold standard" for its diagnosis, and we demonstrated a low reliability of screening test such as the Brown ADD Scales in populations at risk (e.g. acute psychiatric inpatients and parents of children affected by ADHD). Moreover, diagnosis is further complicated by the overlap between the symptoms of adult ADHD and the symptoms of other common psychiatric conditions such as depression and substance abuse. While stimulants are a common treatment for adult patients with ADHD, they are often used as a self-treatment, especially in patients who lack of a correct diagnosis and treatment. Antidepressants may also be effec-

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tive, while cognitive-behavioural skills training and psychotherapy are useful if adjuncts to pharmacotherapy. Addiction thus embodies a key point in differential diagnosis as well as it might be considered an adverse effect of a long duration of untreated illness. As a consequence, it should be accurately checked and weighted during the diagnostic process.

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