NEWSLETTER

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Duca M, et al.
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METHYLPHENIDATE LONG-TERM EFFECTS ON PSYCHIATRIC OUTCOMES IN A SARDINIAN ADHD POPULATION: PRELIMINARY RESULTS FROM THE PROSPECTIVE ADDUCE PROJECT.
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THE UTILITY OF A COMPUTERIZED ALGORITHM BASED ON A MULTI-DOMAIN PROFILE OF MEASURES FOR THE DIAGNOSIS OF ATTENTION DEFICIT/HYPERACTIVITY DISORDER.
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IMPACT OF CO-MORBID ATTENTION-DEFICIT AND HYPERACTIVITY DISORDER ON COGNITIVE FUNCTION IN MALE CHILDREN WITH TOURETTE SYNDROME: A CONTROLLED STUDY.
J Neurol Neurosurg Psychiatry. 2017;88:e35 pag. 61

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THE MULTIPLE PHENOTYPES OF TOURETTE SYNDROME AND ATTENTION-DEFICIT HYPERACTIVITY DISORDER.
Psychiatry Res. 2017;258:611 pag. 63

ISTITUTO DI RICERCHE FARMACOLOGICHE MARIO NEGRI IRCCS

BIBLIOGRAFIA ADHD NOVEMBRE 2017

ADHD Atten Deficit Hyperact Disord. 2017;1-10.

ADHD SYMPTOMS IN HEALTHY ADULTS ARE ASSOCIATED WITH STRESSFUL LIFE EVENTS AND NEGATIVE MEMORY BIAS.

Vrijsen JN, Tendolkar I, Onnink M, et al.

Stressful life events, especially Childhood Trauma, predict ADHD symptoms. Childhood Trauma and negatively biased memory are risk factors for affective disorders. The association of life events and bias with ADHD symptoms may inform about the etiology of ADHD. Memory bias was tested using a computer task in N = 675 healthy adults. Life events and ADHD symptoms were assessed using questionnaires. The mediation of the association between life events and ADHD symptoms by memory bias was examined. We explored the roles of different types of life events and of ADHD symptom clusters. Life events and memory bias were associated with overall ADHD symptoms as well as inattention and hyperactivity/impulsivity symptom clusters. Memory bias mediated the association of Lifetime Life Events, specifically Childhood Trauma, with ADHD symptoms. Negatively biased memory may be a cognitive marker of the effects of Childhood Trauma on the development and/or persistence of ADHD symptoms

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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;1-9.

INTOLERANCE OF UNCERTAINTY IN CHILDREN WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.

Gramszlo C, Fogleman ND, Rosen PJ, et al.

Intolerance of uncertainty (IU) has often been studied in the context of internalizing disorders, but no studies to our knowledge have explored the relation between IU and externalizing disorders. Given the proposed link between IU and emotion regulation, the current study sought to examine levels of IU in an externalizing clinical population with known emotion regulation difficulties attention-deficit/hyperactivity disorder (ADHD). IU levels in this population were compared to a clinical population known to experience elevated levels of IU. Participants in present study were ninety-three children (36 anxiety disorder, 28 ADHD, 29 unaffected children) ages 7-13, who completed the Intolerance of Uncertainty Scale Short Version (IUS). Responses on the IUS were converted to total IU, prospective IU, and inhibitory IU. A linear mixed model analysis of covariance was conducted while controlling for age, sex, and ADHD medications. A significant interaction was observed between diagnostic status and IU scale. Planned contrasts indicated that children with anxiety disorders and ADHD reported significantly higher levels of IU relative to unaffected children, and children with ADHD reported comparable levels of inhibitory IU relative to children with anxiety disorders. The current results contribute to a growing literature on the link between IU and psychopathology. IU appears to be a trans diagnostic construct present among children with internalizing and externalizing disorders, and may be broadly associated with emotion regulation deficits rather than specific disorder symptoms

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Alcohol Clin Exp Res. 2017;41:1953-60.

THE CAUSAL ROLE OF ALCOHOL USE IN ADOLESCENT EXTERNALIZING AND INTERNALIZING PROBLEMS: A MENDELIAN RANDOMIZATION STUDY.

Chao M, Li X, McGue M.

BACKGROUND: The co-occurrence of alcohol use and externalizing/internalizing problems threatens adolescents' mental health. Research on whether alcohol use and these problems are causal and the direction of the potential causal relationships is needed to understand the mechanisms of the co-occurrence.
METHODS: A Mendelian randomization analysis was conducted in which the aldehyde dehydrogenase 2 (ALDH2) rs671 polymorphism was used as an instrumental variable for alcohol use phenotypes. In total, 1,608 Chinese adolescents (mean age 14.11 ± 1.83 years) were genotyped for the ALDH2 rs671 polymorphism. Three externalizing problems (aggression, delinquency, and attention problems) were measured with the Youth Self-Report inventory, and 2 internalizing problems (depression and anxiety) were measured with the self-reported Children's Depression Inventory and the Trait subscale of the State-Trait Anxiety Inventory.
RESULTS: Alcohol use was positively associated with all 3 externalizing and 2 internalizing problems, and the ALDH2 polymorphism had a significant effect on alcohol use. Aggression and attention problems were also significantly affected by the ALDH2 polymorphism, whereas no significant association was observed between the ALDH2 polymorphism and delinquency, anxiety, or depression.
CONCLUSIONS: The results suggest that alcohol use is a cause of adolescent aggression and attention problems but not adolescent delinquency, anxiety, or depression.

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Allergy Eur J Allergy Clin Immunol. 2017.

INCREASED ATTENTION-DEFICIT/HYPERACTIVITY SYMPTOMS IN ATOPIC DERMATITIS ARE ASSOCIATED WITH HISTORY OF ANTIHISTAMINE USE.

Schmitt J, Buske-Kirschbaum A, Tesch F, et al.

Background: Epidemiologic evidence indicates a relevant association between atopic dermatitis (AD) and attention-deficit/hyperactivity disorder (ADHD). Underlying mechanisms and ways to best identify subgroups of AD patients at risk for ADHD are poorly understood.

Aims of the study: To compare sociodemographic, clinical and psychosocial characteristics of children with AD, ADHD, comorbid AD/ADHD and age-matched healthy controls and to investigate aspects of AD related to ADHD symptoms.
Methods: Applying a factorial design, we investigated 4 groups of children aged 6-12 years: AD-only (ie, without ADHD), ADHD-only (ie, without AD), AD + ADHD and healthy controls (HC; ie, no AD/no ADHD). Using validated instruments, ADHD symptoms and other behavioural problems, quality of life, parenting stress and sleeping problems were compared between groups. In children with AD-only, clinical signs (objective SCORAD), symptoms (POEM, VAS pruritus, VAS sleeping problems) and previous treatment of AD were assessed to investigate disease patterns related to ADHD symptoms.
Results: Compared to HC (n = 47), children with AD-only (n = 42), ADHD-only (n = 34) and comorbid AD + ADHD (n = 31) had significantly increased behavioural problems and decreased quality of life. Children with AD-only had significantly higher levels of ADHD symptoms than HC. In children with AD-only, previous use of antihistamines was significantly associated with increased ADHD symptoms (OR 1.88; 95% CI 1.04-3.39). Current clinical signs and AD symptoms were unrelated to the level of ADHD symptoms.
Conclusions: Even if the clinical diagnosis of ADHD is excluded, children with AD show increased levels of ADHD symptoms. Further investigations need to determine whether early antihistamine exposure is a major risk factor for ADHD or a surrogate for previous AD severity and/or associated sleeping problems

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Ann Nutr Metab. 2017;71:1030.

DIET AND CHILDREN WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER (ADHD)-A PILOT INTERVENTION STUDY FOCUSING ON COMPLIANCE AND SYMPTOMS.

Birgisdottir BE, Lauth B, Geirsdottir Ã, et al.

Background and objectives: The potential effect of food on Attention deficit hyperactivity disorder (ADHD) symptoms has long been debated. The aim of this pilot study was primarily to investigate compliance to two diets of interest, the healthy diet and the temporary few foods diet (few allergens) and secondary evaluate their effects on ADHD symptoms.
Methods: Participants were children who had been diagnosed with ADHD at the two main psychiatric centers for children in Reykjavik, with 29 children randomized into three groups: healthy diet (n=10), few foods diet (n=10) and a control group (n=9). A three-day food diary and questionnaires for both parents and teachers gave background information and symptoms. The same questionnaires were answered five weeks later as well as questions regarding the participation. A blinded physician interviewed the children and parents before and after the intervention. Compliance checklists were designed for the intervention period. Full participation rate was 68%.
Results: Baseline diet was not in line with dietary recommendations. Compliance to the diets was generally good (70-80%), although most children found it hard to follow the few foods diet and four dropped out. Using ADHD rating scale (ARS) the parents' total score decreased similarly on both diets (median from 35 to 27) or by 25% ($p<0.05$). Teachers found no change on ARS nor on Achenbach's Teacher Rating Form after the healthy diet, but significant improvement of symptoms were observed after the few foods diet ($p=.027$). No change was seen in the control group. The psychiatrist also found differences between groups ($p<0.05$).
Conclusions: With good support, compliance was generally good. Parents reported a decrease in symptoms on both diets, while teachers only reported improvements for children on the few foods diet. Diet of children with ADHD can be substantially improved and nutritional status and food sensitivity should be examined at diagnosis. However, further studies are needed

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Ann Trop Med Public Health. 2017;10:1341-44.

THE EFFECT OF SPACE FACE GAMES ON THE AMOUNT OF CHILDREN ATTENTION WITH ATTENTION DEFICIT HYPERACTIVITY DISORDERS.

Shahmoradi Z, Maghsoudi J, Najafi M, et al.

Introduction: As ever play therapy using a special toy which is produced with therapeutic target in children with attention deficit hyperactivity disorders (ADHDs) has not been conducted, this study was carried out with the aim to determine the effect of space face games on the attention of children with ADHDs.

Materials and Methods: In this research, 72 children with ADHDs referred to Isfahan's Noor psychiatric clinic were randomly placed in two test and control groups. Attention level of both groups was evaluated using continuous performance test before and after the intervention. The space face games in the test group were used for 16 sessions. Statistical analysis of data was conducted using descriptive and analytical statistics in SPSS Software Version 18.

Findings: The average score of attention had no significant difference between the two groups before the intervention, but the number of correct answer in the test group was significantly more than the control group and the number of provided errors and the number of removed errors were significantly lower than the control group immediately after the intervention.

Conclusion: Space face games are effective in the promotion of attention in children with ADHDs

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Basic Clin Neurosci. 2017;8:419-27.

EMOTIONAL FACE RECOGNITION IN CHILDREN WITH ATTENTION DEFICIT/HYPERACTIVITY DISORDER: EVIDENCE FROM EVENT RELATED GAMMA OSCILLATION.

Razavi MS, Tehranidoost M, Ghassemi F, et al.

Introduction: Children with attention-deficit/hyperactivity disorder (ADHD) have some impairment in emotional relationship which can be due to problems in emotional processing. The present study investigated neural correlates of early stages of emotional face processing in this group compared with typically developing children using the Gamma Band Activity (GBA).

Methods: A total of 19 children diagnosed with ADHD (Combined type) based on DSM-IV classification were compared with 19 typically developing children matched on age, gender, and IQ. The participants performed an emotional face recognition while their brain activities were recorded using an event-related oscillation procedure.

Results: The results indicated that ADHD children compared to normal group showed a significant reduction in the gamma band activity, which is thought to reflect early perceptual emotion discrimination for happy and angry emotions ($P < 0.05$).

Conclusion: The present study supports the notion that individuals with ADHD have some impairments in early stage of emotion processing which can cause their misinterpretation of emotional faces

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Biol Psychiatry. 2017;82:669-78.

BEHAVIORAL AND NEURAL SUSTAINED ATTENTION DEFICITS IN BIPOLAR DISORDER AND FAMILIAL RISK OF BIPOLAR DISORDER.

Pagliaccio D, Wiggins JL, Adleman NE, et al.

Background Few neuroimaging studies compare individuals affected with bipolar disorder (BP), at high familial risk of BP, and at low risk to identify endophenotypes for BP. None have examined variability in attention, despite promising behavioral work in this area. We used functional magnetic resonance imaging (fMRI) methods uniquely powered to compare the neural correlates of attention variability in these three groups.

Methods The present study examined 8- to 25-year-old individuals (n = 106) who completed an fMRI attention task: 24 with BP, 29 at risk based on a first-degree relative with BP, and 53 healthy, low-risk individuals. Group differences in intrasubject variability in reaction time were examined, and a sophisticated

fMRI analytic approach was used to quantify precisely trialwise associations between reaction time and brain activity. The latter has not been examined previously in BP or risk of BP.
Results Relative to healthy individuals, those with BP or at risk for BP exhibited increased reaction time variability (F2,102 = 4.26, p =.02, Î·p2 =.08). Importantly, we identified blunted relationships between trialwise variation in reaction time and brain activity in the inferior and middle frontal gyri, precuneus, cingulate cortex, caudate, and postcentral gyrus (all regions: p <.001, Î·p2 >.06) in both at-risk and BP individuals compared with healthy, low-risk individuals. This blunting partially mediated group differences in reaction time variability (Î² =.010, 95% confidence interval 0.002 to 0.020, Sobel Z = 2.08, p =.038).
Conclusions Blunting in key frontal, cingulate, and striatal areas was evident in unaffected, at-risk individuals and in euthymic BP patients. Elucidating such novel neural endophenotypes can facilitate new approaches to BP prediction, diagnosis, and prevention

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Biomarker Insights. 2015;10:33-38.
POLYMORPHISM IN VARIABLE NUMBER OF TANDEM REPEATS OF DOPAMINE D4 GENE IS A GENETIC RISK FACTOR IN ATTENTION DEFICIT HYPERACTIVE EGYPTIAN CHILDREN: PILOT STUDY.
Shahin O, Meguid NA, Raafat O, et al.
INTRODUCTION: The variable number of tandem repeats (VNTR) of the dopamine receptor D4 (DRD4) gene among humans may elucidate individual differences in susceptibility to neuropsychiatric diseases. Dopamine dysfunction may be involved with Attention Deficit Hyperactivity Disorder (ADHD) symptoms. In this study, we report the association between the phenotype of ADHD, a condition characterized by inattentiveness, hyperactivity, and impulsiveness, and a 48-base pair VNTR in exon 3 of the DRD4 polymorphism.
SUBJECTS AND METHODS: We used a case control approach conducted on 29 ADHD and 31 ethnically matched control Egyptian children (ages 6-12 years). Cases were assessed by a psychiatric semi-structured interview and the Conners' Parent Rating Scale. VNTR polymorphisms of the DRD4 gene were done by touchdown PCR program using exon 3-specific primers followed by agarose gel electrophoresis.
RESULTS: We observed a significant association between the existence of D4.4 allele of DRD4 and ADHD (P, 0.002); 6.9% of cases showed a single D4.4 and 10.3% showed a double D4.4 as compared to controls in whom D4.4 has never been detected.
CONCLUSION: Children with smaller number of repeat alleles (two to four repeats) of the DRD4 gene have higher possibility to develop ADHD in Egyptian children.

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BMJ Open. 2017;7.
ECONOMIC VOLATILITY IN CHILDHOOD AND SUBSEQUENT ADOLESCENT MENTAL HEALTH PROBLEMS: A LONGITUDINAL POPULATION-BASED STUDY OF ADOLESCENTS.
Bøe T, Skogen JC, Sivertsen B, et al.
Objective The aim of the current paper was to investigate the association between the patterns of duration, timing and sequencing of exposure to low family income during childhood, and symptoms of mental health problems in adolescence.
Setting Survey administered to a large population-based sample of Norwegian adolescents.
Participants Survey data from 9154 participants of 16-19 years age (53% participation rate; 52.7% girls) were linked to registry-based information about childhood family income from tax return data.
Outcome measures Mental health outcomes were symptoms of emotional, conduct, hyperactivity, peer problems and general mental health problems measured with the Strengths and Difficulties Questionnaire, symptoms of depression measured with Short Mood and Feelings Questionnaire and symptoms of attention-deficit/hyperactivity disorder (ADHD) measured with the Adult ADHD Self-Report Scale.
Results Latent class analysis and the BCH approach in Mplus were used to examine associations between patterns of poverty exposure and mental health outcomes. Four latent classes of poverty exposure emerged from the analysis. Participants moving into poverty (2.3%), out of poverty (3.5%) or those chronically poor

(3.1%) had more symptoms of mental health problems (Cohen's d=16-.50) than those with no poverty exposure (91.1%). This pattern was, however, not found for symptoms of ADHD. The pattern of results was confirmed in robustness checks using observed data.
Conclusions Exposure to poverty in childhood was found to be associated with most mental health problems in adolescence. There was no strong suggestion of any timing or sequencing effects in the patterns of associations

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Cereb Cortex. 2017;27:4624-34.

WHAT CAN CORTICAL DEVELOPMENT IN ATTENTION-DEFICIT/ HYPERACTIVITY DISORDER TEACH US ABOUT THE EARLY DEVELOPMENTAL MECHANISMS INVOLVED?

Ambrosino S, de ZP, Wierenga LM, et al.

Studies of Attention-Deficit/Hyperactivity Disorder (ADHD) have shown developmental changes in the cortical mantle. Different dimensions of cortical morphology, such as surface area and thickness, relate to different neurodevelopmental mechanisms. As such, studying multiple dimensions may inform us about the developmental origins of ADHD. Furthermore, results from existing longitudinal samples await replication. Therefore, we conducted a longitudinal study of multiple cortical dimensions in a sizable, independent ADHD sample. We analyzed 297 anatomical MRI scans from two matched groups of 94 subjects with ADHD and 94 controls, aged 6-28 years. We estimated the developmental trajectories of cortical volume, surface, thickness and gyrification for 68 regions using mixed-effects regression analysis. Subjects with ADHD had smaller overall cortical volume, predominantly driven by decreases in frontal lobe volume that were associated with reduced surface area and gyrification. Nearly all decreases were stable across development. Only a few decreases survived stringent Bonferroni correction for multiple comparisons, with the smallest detectable Cohen's d |0.43|. There were no between-group differences in cortical thickness, or in subcortical volumes. Our results suggest that ADHD is associated with developmentally persistent reductions in frontal cortical volume, surface area, and gyrification. This may implicate early neurodevelopmental mechanisms regulating cortical expansion and convolution in ADHD

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Child Adolesc Ment Health. 2017.

THE PRESENTATION OF DEPRESSION SYMPTOMS IN ATTENTION-DEFICIT/HYPERACTIVITY DISORDER: COMPARING CHILD AND PARENT REPORTS.

Fraser A, Cooper M, Agha SS, et al.

Background: Attention-deficit/hyperactivity disorder (ADHD) frequently co-occurs with depression, and outcomes are poor when both are present. Little is known about whether depression symptoms present differently in ADHD compared to the general population, or how reliable young people with ADHD are at reporting these symptoms. This study aimed to describe depression symptoms in a clinical ADHD sample compared to a population sample, and compare self-reports of depression symptoms with parent-reports.
Methods: Two hundred and forty-nine children with ADHD and their parents completed follow-up questionnaires around 5 years after taking part in a Cardiff University ADHD study. Child depression symptoms were measured using parent- and child-reported Mood and Feelings Questionnaires (MFQ) and compared to a population sample with MFQ data (n = 1460). Within both samples, child- and parent-reported depression symptoms were compared.
Results: Although the profile of depression symptoms was similar between young people with ADHD and those in the general population, depression symptoms were much more common in the ADHD sample (parent-rated MFQ score = 24.52 vs. 9.39; child-rated = 21.02 vs. 11.86). The most common symptoms in both samples included irritability, restlessness and concentration difficulties, with core depression symptoms such as feeling miserable/unhappy also prominent. Within the ADHD sample, but not the population sample, children reported depression symptoms less frequently than their parents.

Conclusions: Young people with ADHD are at high risk of experiencing symptoms of depression but may under-report the severity of their symptoms. Obtaining parent reports of depression symptoms in this group may be important to avoid missing key indicators of risk

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Child Adolesc Ment Health. 2017;22:216-23.

TRAIT EMOTIONAL INTELLIGENCE IN A SAMPLE OF EGYPTIANÂ CHILDREN WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER.

Abo EE, Hassan GAM, Sabry W, et al.

Background: The link between types and severity of attention deficit hyperactivity disorder (ADHD) symptoms and trait emotional intelligence (TEI) is still underinvestigated, especially in children. We aimed to examine the relationship between TEI and ADHD symptoms in a sample of Egyptian children.

Method: The study included 50 children with ADHD, who were compared on the basis of their TEI and contrasted with 25 matched healthy controls. They were subjected to the Arabic version of the following scales: Connors scale 3rd edition, parent rating form, Kiddie-Schedule for affective disorders and Schizophrenia present and Lifetime Version (K-SADS-PL), Stanford Binet intelligence scale, 4th edition and Trait Emotional Intelligence Child form (TEI) and a semistructured clinical data sheet for sociodemographic data.

Results: Using TEI scale, the control group was shown to have higher scores in TEI than cases, there was a high significant difference with regards to eight of nine TEI facets together with the TEI global score. Moreover, the control group significantly outperformed ADHD children with mixed and hyperactive subtypes on TEI global score in all facets except for adaptability. Meanwhile, the inattentive group performed significantly poorer than those in the control group on TEI global score, adaptability, emotional expression, self-motivation and emotion regulation facets. Trait Emotional Intelligence was negatively correlated with four of ADHD symptom groups assessed by Connors test, namely; impulsivity, cognitive, social problem, and emotional liability symptoms. However, Impulsivity was negatively correlated with all the domains of TEI except for adaptability and emotional expression. On the other hand, oppositional symptoms did not show a significant correlation with any of the TEI facets.

Conclusions: Trait emotional intelligence is highly impaired in children with ADHD and emotional deficits are corner stone features of that disorder, low impulsivity facet of TEI is highly correlated with social problems and poor peer relations

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Child Neuropsychol. 2018;24:82-105.

ARE SLUGGISH COGNITIVE TEMPO SYMPTOMS ASSOCIATED WITH EXECUTIVE FUNCTIONING IN PRESCHOOLERS?

Tamm L, Brenner SB, Bamberger ME, et al.

The aim of this study is to investigate whether sluggish cognitive tempo (SCT) symptoms are associated with neurocognitive task performance and ratings of real-world executive functioning (EF) in preschoolers at risk for attention-deficit/hyperactivity disorder (ADHD). The associations between parent- and teacher-rated SCT symptoms and neuropsychological task performance and ratings of EF in 61 4-year-old preschool children (51 boys, 10 girls) with self-regulation difficulties were examined, with regression analyses controlling for the effects of ADHD inattention symptoms. In the study sample, higher teacher-rated SCT symptoms are significantly associated with poorer performance on tasks of visual-perceptual abilities, auditory and visual attention, sustained and selective attention, inhibitory control, pre-numerical/numerical concepts, and slower processing speed, but SCT symptoms are not significantly associated with working memory, attention shifting or cognitive flexibility when controlling for ADHD inattention. Higher parent-rated SCT symptoms are significantly associated with visual-perceptual abilities. ADHD inattention symptoms are more strongly associated than SCT with daily life EF ratings; neither parent- nor teacher-rated SCT symptoms are significantly associated with daily life ratings of inhibition, working memory, or planning/organization after controlling for ADHD inattention. This study suggests that SCT symptoms contribute to EF deficits at least on neurocognitive tasks assessing visual-perceptual/spatial abilities, attention to detail and processing

speed, as observed in this sample of young children at risk for ADHD, and may be an important intervention target

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Child Health Care. 2017;46:344-55.

CLINICIAN DISPARITIES IN ANXIETY AND TRAUMA SCREENING AMONG CHILDREN WITH ADHD: A PILOT STUDY.

Spitzer J, Schrager SM, Imagawa KK, et al.

The objective of this study was to determine the rate of clinician screening for anxiety disorders or trauma when diagnosing childhood ADHD and investigate the roles of clinical setting and clinician discipline. Data were retrospectively collected in general pediatric (GP) and mental health (MH) settings. Screening rates were compared between visits in GP vs. MH setting and with a developmental–behavioral pediatrician (DBP) vs. visits without a DBP. Analysis of 200 charts revealed an overall 44% documentation rate of anxiety or trauma history screen. DBPs were responsible for 53 (26.5% of) cases; with DBP involvement, screening rates for anxiety or trauma rose to 77%, with significant variation by setting (OR = 5.27, $p < 0.001$) and clinician type (OR = 2.64, $p < 0.001$). Clinicians in the GP setting document screening for anxiety or trauma history significantly less often than clinicians in the MH setting. DBPs have an opportunity to improve the rate of anxiety and trauma screening when evaluating ADHD.

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Clin Psychopharmacol Neurosci. 2017;15:410-12.

HICCUP DUE TO ARIPIPRAZOLE PLUS METHYLPHENIDATE TREATMENT IN AN ADOLESCENT WITH ATTENTION DEFICIT AND HYPERACTIVITY DISORDER AND CONDUCT DISORDER: A CASE REPORT.

Kutuk MO, Guler G, Tufan AE, et al.

Our case had hiccups arising in an adolescent with the attention deficit and hyperactivity disorder (ADHD) and conduct disorder (CD) after adding aripiprazole treatment to extended-release methylphenidate. Actually, antipsychotics are also used in the treatment of hiccups, but studies suggest that they can cause hiccups as well. Within 12 hours of taking 2.5 mg aripiprazole added to extended-release methylphenidate at a dose of 54 mg/day, 16-year-old boy began having hiccups in the morning, which lasted after 3-4 hours. As a result, aripiprazole was discontinued and methylphenidate was continued alone because we could not convince the patient to use another additional drug due to this side effect. Subsequently, when his behavior got worsened day by day, his mother administered aripiprazole alone again at the dose of 2.5 mg/day at the weekend and continued treatment because hiccup did not occur again. But when it was administered with methylphenidate on Monday, hiccup started again next morning and lasted one hour at this time. In conclusion, we concluded that concurrent use of methylphenidate and aripiprazole in this adolescent led to hiccups

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CNS Spectr. 2017;22:103.

EFFICACY AND SAFETY OF HLD200 IN CHILDREN WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER: RESULTS FROM A PIVOTAL PHASE 3 TRIAL.

Arnold V, Pliszka S, Marraffino A, et al.

OBJECTIVE: Evening-dosed HLD200 delays the initial release of methylphenidate by approximately 8-10 hours, targeting the onset of clinically meaningful treatment effect upon awakening and lasting to the evening. The objective was to determine whether HLD200 improves control of ADHD symptoms, and at-home early morning and evening functioning versus placebo in children with attention-deficit/hyperactivity disorder (ADHD). Safety and tolerability were also assessed.

METHODS: This was a pivotal, randomized, double-blind, multicenter, placebo-controlled, parallel-group, phase 3 trial of HLD200 in children (6-12 years) with ADHD (NCT02520388). Subjects had current or prior response on methylphenidate. Following a screening period of 2 weeks with a 3-to 7-day washout, subjects were randomized (1:1) to HLD200 or placebo once-daily each evening for 3 weeks. After 1 week, the initial

40 mg dose of HLD200 was titrated in 20 mg weekly increments to 60 mg and 80 mg, as tolerated, with a one-step downtitration permitted. The primary efficacy measure was the ADHD Rating Scale (ADHD-RS-IV) Total Score following 3 weeks of treatment. The key secondary efficacy measures were the Before School Functioning Questionnaire (BSFQ) and Parent Rating of Evening and Morning Behavior-Revised, Morning (PREMB-R AM) and Evening (PREMB-R PM) subscales following 3 weeks of treatment. Safety measures included treatmentemergent adverse events (TEAEs), with a focus on sleep and appetite.
RESULTS: Of 163 children enrolled across 22 sites, 161 were included in the intent-to-treat population. After 3 weeks of treatment, children on HLD200 achieved a significant improvement versus those on placebo in ADHD symptoms (least-squares [LS] mean ADHDRS-IV: 24.1 vs 31.2; p= 0.002), at-home early morning functioning (LS mean BSFQ: 18.7 vs 28.4; p< 0.001; LS mean PREMB-R AM: 2.1 vs 3.6; p <0.001), and at-home evening functioning (LS mean PREMB-R PM: 9.4 vs 12.2; p= 0.002). There were no serious TEAEs, and all reported TEAEs were consistent with the known effects of methylphenidate. All sleeprelated TEAEs were transient and mild or moderate in severity.
CONCLUSIONS: Following daily evening administration, HLD200 was well tolerated and demonstrated significant improvements in ADHD symptoms and both at-home early morning and evening functioning versus placebo in children with ADHD

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Congenit Anomal. 2017;57:A2-A3.
THE USE OF ADHD MEDICATION DURING PREGNANCY.
Muraoka K, Murakami Y, Nagata K, et al.
Attention deficit hyperactivity disorder (ADHD) is a common neuropsychological disorder characterized by symptoms of inattention, distractibility, and impulsion. It was considered that the symptom was limited during a childhood condition, however, the prevalence of ADHD among adults grew over the last decade. It is estimated that between 30% and 70% of children with ADHD will still have the symptoms even if they become adults. Based on the Diagnostic and Statistical Manual of Mental Disorders-5th edition, approximately 5.0% of children and 2.5% of adults might suffer from the disorder. First intervention and strategies with ADHD are environmental modifications and behavior management, but pharmacotherapy is considered in the case that having a difficulty in introduction of these treatments and showing insufficient effects. Also in the severe case, pharmacotherapy is used in the early period. In Japan, the stimulant medication methylphenidate is considered as first-line therapy for treatment in adults, and the non-stimulant medication atomoxetine is also approved for adult ADHD, and could be used as first-line therapy for certain patients. The non-stimulant medication guanfacine, a selective alpha-2A adrenoceptor agonist, is also approved only for children in 2017. The number of children diagnosed with ADHD has risen dramatically over the past two decades, and some remain on treatment into adulthood. In the report of Denmark, the use of ADHD medication among women of childbearing age has increased from 5 to 533 per 100, 000 person-years between 1999 and 2010 (Haervig et al., Pharmacoepidemiol Drug Saf 2014, 23: 526-533). Therefore, there is much potential for inadvertent exposure to these medications. It is thus important to monitor the use of ADHD medication during pregnancy from the viewpoint of the proper use of pharmaceutical products

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Crit Care Med. 2017;45:1742-50.
NEUROBIOLOGIC CORRELATES OF ATTENTION AND MEMORY DEFICITS FOLLOWING CRITICAL ILLNESS IN EARLY LIFE.
Schiller RM, IJsselstijn H, Madderom MJ, et al.
OBJECTIVES: Survivors of critical illness in early life are at risk of long-term-memory and attention impairments. However, their neurobiologic substrates remain largely unknown.
DESIGN: A prospective follow-up study.
SETTING: Erasmus MC-Sophia Children's Hospital, Rotterdam, the Netherlands.
PATIENTS: Thirty-eight school-age (8-12 yr) survivors of neonatal extracorporeal membrane oxygenation and/or congenital diaphragmatic hernia with an intelligence quotient greater than or equal to 80 and a below average score (z score ≤ -1.5) on one or more memory tests.

INTERVENTIONS: None.
MEASUREMENTS AND MAIN RESULTS: Intelligence, attention, memory, executive functioning, and visuospatial processing were assessed and compared with reference data. White matter microstructure and hippocampal volume were assessed using diffusion tensor imaging and structural MRI, respectively. Global fractional anisotropy was positively associated with selective attention (β = 0.53; p = 0.030) and sustained attention (β = 0.48; p = 0.018). Mean diffusivity in the left parahippocampal region of the cingulum was negatively associated with visuospatial memory, both immediate (β = -0.48; p = 0.030) and delayed recall (β = -0.47; p = 0.030). Mean diffusivity in the parahippocampal region of the cingulum was negatively associated with verbal memory delayed recall (left: β = -0.52, p = 0.021; right: β = -0.52, p = 0.021). Hippocampal volume was positively associated with verbal memory delayed recall (left: β = 0.44, p = 0.037; right: β = 0.67, p = 0.012). Extracorporeal membrane oxygenation treatment or extracorporeal membrane oxygenation type did not influence the structure-function relationships.
CONCLUSIONS: Our findings indicate specific neurobiologic correlates of attention and memory deficits in school-age survivors of neonatal extracorporeal membrane oxygenation and congenital diaphragmatic hernia. A better understanding of the neurobiology following critical illness, both in early and in adult life, may lead to earlier identification of patients at risk for impaired neuropsychological outcome with the use of neurobiologic markers

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Dev Cognitive Neurosci. 2017;28:12-20.

AN ELECTROPHYSIOLOGICAL INVESTIGATION OF REINFORCEMENT EFFECTS IN ATTENTION DEFICIT/HYPERACTIVITY DISORDER: DISSOCIATING CUE SENSITIVITY FROM DOWN-STREAM EFFECTS ON TARGET ENGAGEMENT AND PERFORMANCE.

Chronaki G, Soltesz F, Benikos N, et al.

Objective Neural hypo-sensitivity to cues predicting positive reinforcement has been observed in ADHD using the Monetary Incentive Delay (MID) task. Here we report the first study using an electrophysiological analogue of this task to distinguish between (i) cue related anticipation of reinforcement and downstream effects on (ii) target engagement and (iii) performance in a clinical sample of adolescents with ADHD and controls.
Methods Thirty-one controls and 32 adolescents with ADHD aged 10 16 years performed the electrophysiological (e)-MID task in which preparatory cues signal whether a response to an upcoming target will be reinforced or not under three conditions; positive reinforcement, negative reinforcement (response cost) and no consequence (neutral). We extracted values for both cue-related potentials known to be, both, associated with response preparation and modulated by reinforcement (Cue P3 and Cue CNV) and target-related potentials (target P3) and compared these between ADHD and controls.
Results ADHD and controls did not differ on cue-related components on neutral trials. Against expectation, adolescents with ADHD displayed Cue P3 and Cue CNV reinforcement-related enhancement (versus neutral trials) compared to controls. ADHD individuals displayed smaller target P3 amplitudes and slower and more variable performance but effects were not modulated by reinforcement contingencies. When age, IQ and conduct problems were controlled effects were marginally significant but the pattern of results did not change.
Discussion ADHD was associated with hypersensitivity to positive (and marginally negative) reinforcement reflected on components often thought to be associated with response preparation however these did not translate into improved attention to targets. In the case of ADHD, upregulated CNV may be a specific marker of hyper-arousal rather than an enhancement of anticipatory attention to upcoming targets. Future studies should examine the effects of age, IQ and conduct problems on reinforcement sensitivity in ADHD

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Dev Cognitive Neurosci. 2017;28:21-28.

AN EVENT-RELATED POTENTIAL INVESTIGATION OF THE ACUTE EFFECTS OF AEROBIC AND COORDINATIVE EXERCISE ON INHIBITORY CONTROL IN CHILDREN WITH ADHD.

Ludyga S, Brand S, Gerber M, et al.

The current body of evidence suggests that an aerobic exercise session has a beneficial effect on inhibitory control, whereas the impact of coordinative exercise on this executive function has not yet been examined in children with ADHD. Therefore, the present study aims to investigate the acute effects of aerobic and coordinative exercise on behavioral performance and the allocation of attentional resources in an inhibitory control task. Using a cross-over design, children with ADHD-combined type and healthy comparisons completed a Flanker task before and after 20 min moderately-intense cycling exercise, coordinative exercise and an inactive control condition. During the task, stimulus-locked event-related potentials were recorded with electroencephalography. Both groups showed an increase of P300 amplitude and decrease of reaction time after exercise compared to the control condition. Investigating the effect of exercise modality, aerobic exercise led to greater increases of P300 amplitude and reductions in reaction time than coordinative exercise in children with ADHD. The findings suggest that a single exercise bout improves inhibitory control and the allocation of attentional resources. There were some indications that an aerobic exercise session seems to be more efficient than coordinative exercise in reducing the inhibitory control deficits that persist in children with ADHD

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Dev Neurorehabilitation. 2017;1-10.

THE RELATION BETWEEN EMOTIONAL INTELLIGENCE AND RESILIENCE IN AT-RISK POPULATIONS.

McCrimmon AW, Climie EA, Huynh S.

Purpose: Resilience factors and their relation to emotional intelligence (EI) as a potential strength for children with attention-deficit/hyperactivity disorder (ADHD) or high-functioning autism spectrum disorder (HFASD) were investigated. Children with either ADHD or HFASD were hypothesized to demonstrate reduced EI and differential relations between EI and resilience as compared to typically developing (TD) children.

Methods: Fifty-four children aged 8.12 years (18 with ADHD, 18 with HFASD, and 18 TD controls) completed the Resilience Scales for Children and Adolescents and BarOn Emotional Quotient Inventory. Differences between groups (analysis of variance) and unique relations among the variables (correlation) for each group were examined.

Results: No group differences; however, unique relations between the variables were found within each sample.

Conclusions: EI may be a unique area of interest for clinical populations and an important consideration in the development and implementation of interventions to capitalize upon inherent strengths. Implications of these results for intervention are discussed

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Eur Child Adolesc Psychiatry. 2017;1-9.

TRAUMA EXPOSURE IN CHILDREN WITH AND WITHOUT ADHD: PREVALENCE AND FUNCTIONAL IMPAIRMENT IN A COMMUNITY-BASED STUDY OF 6-8-YEAR-OLD AUSTRALIAN CHILDREN.

Schilpzand EJ, Sciberras E, Alisic E, et al.

Both ADHD and trauma exposure are common childhood problems, but there are few empirical data regarding the association between the two conditions. The aims of this study were to compare lifetime prevalence of trauma exposure in children with and without ADHD, and to explore the association between trauma exposure and outcomes in children with ADHD. Children aged 6-8 years with ADHD (n = 179) and controls (n = 212) recruited from 43 schools were assessed for ADHD, trauma exposure and comorbid mental health disorders using the Diagnostic Interview Schedule for Children IV. Outcome data were collected by direct child assessment, parent report and teacher-report, and included ADHD symptom severity, internalizing and externalizing problems, quality of life, and academic functioning. Logistic and linear regression models were used to examine differences adjusted for child and family socio-demographics.

Children with ADHD were more likely than controls to have ever experienced a traumatic event (27 vs 16%; OR: 1.99; 95% CI 1.21, 3.27). This difference remained significant in the adjusted model (OR: 1.76, 95% CI 1.03, 3.01) accounting for child factors (age and gender) and family socio-demographic factors (parent age, parent high school completion and single parent status). Among those with ADHD, trauma-exposed children had higher parent-reported ADHD severity and more externalizing problems than non-exposed children, however, this effect attenuated in adjusted model. Children with ADHD were more likely to have experienced a traumatic event than controls. The high prevalence of trauma exposure in our sample suggests that clinicians should evaluate for trauma histories in children presenting with ADHD

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Eur Child Adolesc Psychiatry. 2017;1-13.

A 6-MONTH FOLLOW-UP OF AN RCT ON BEHAVIORAL AND NEUROCOGNITIVE EFFECTS OF NEUROFEEDBACK IN CHILDREN WITH ADHD.

Geladé K, Janssen TWP, Bink M, et al.

To assess the long-term effects of neurofeedback (NFB) in children with attention deficit hyperactivity disorder (ADHD), we compared behavioral and neurocognitive outcomes at a 6-month naturalistic follow-up of a randomized controlled trial on NFB, methylphenidate (MPH), and physical activity (PA). Ninety-two children with a DSM-IV-TR ADHD diagnosis, aged 7-13, receiving NFB (n = 33), MPH (n = 28), or PA (n = 31), were re-assessed 6-months after the interventions. NFB comprised theta/beta training on the vertex (cortical zero). PA comprised moderate to vigorous intensity exercises. Outcome measures included parent and teacher behavioral reports, and neurocognitive measures (auditory oddball, stop-signal, and visual spatial working memory tasks). At follow-up, longitudinal hierarchical multilevel model analyses revealed no significant group differences for parent reports and neurocognitive measures (p = .058-.997), except for improved inhibition in MPH compared to NFB (p = .040) and faster response speed in NFB compared to PA (p = .012) during the stop-signal task. These effects, however, disappeared after controlling for medication use at follow-up. Interestingly, teacher reports showed less inattention and hyperactivity/impulsivity at follow-up for NFB than PA (p = .004-.010), even after controlling for medication use (p = .013-.036). Our findings indicate that the superior results previously found for parent reports and neurocognitive outcome measures obtained with MPH compared to NFB and PA post intervention became smaller or non-significant at follow-up. Teacher reports suggested superior effects of NFB over PA; however, some children had different teachers at follow-up. Therefore, this finding should be interpreted with caution. Clinical trial registration Train your brain and exercise your heart? Advancing the treatment for Attention Deficit Hyperactivity Disorder (ADHD), Ref. no. NCT01363544, https://clinicaltrials.gov/show/NCT01363544

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Eur Child Adolesc Psychiatry. 2017;1-13.

A COMPARISON OF THE CLINICAL EFFECTIVENESS AND COST OF SPECIALISED INDIVIDUALLY DELIVERED PARENT TRAINING FOR PRESCHOOL ATTENTION-DEFICIT/HYPERACTIVITY DISORDER AND A GENERIC, GROUP-BASED PROGRAMME: A MULTI-CENTRE, RANDOMISED CONTROLLED TRIAL OF THE NEW FOREST PARENTING PROGRAMME VERSUS INCREDIBLE YEARS.

Sonuga-Barke EJS, Barton J, Daley D, et al.

The objective of this study is to compare the efficacy and cost of specialised individually delivered parent training (PT) for preschool children with attention-deficit/hyperactivity disorder (ADHD) against generic group-based PT and treatment as usual (TAU). This is a multi-centre three-arm, parallel group randomised controlled trial conducted in National Health Service Trusts. The participants included in this study were preschool children (33-54 months) fulfilling ADHD research diagnostic criteria. New Forest Parenting Programme (NFPP)-12-week individual, home-delivered ADHD PT programme; Incredible Years (IY)-12-week group-based, PT programme initially designed for children with behaviour problems were the interventions. Primary outcome-Parent ratings of child's ADHD symptoms (Swanson, Nolan & Pelham Questionnaire-SNAP-IV). Secondary outcomes-teacher ratings (SNAP-IV) and direct observations of ADHD symptoms and parent/teacher ratings of conduct problems. NFPP, IY and TAU outcomes were measured at

baseline (T1) and post treatment (T2). NFPP and IY outcomes only were measured 6 months post treatment (T3). Researchers, but not therapists or parents, were blind to treatment allocation. Analysis employed mixed effect regression models (multiple imputations). Intervention and other costs were estimated using standardized approaches. NFPP and IY did not differ on parent-rated SNAP-IV, ADHD combined symptoms [mean difference - 0.009 95% CI (- 0.191, 0.173), p = 0.921] or any other measure. Small, non-significant, benefits of NFPP over TAU were seen for parent-rated SNAP-IV, ADHD combined symptoms [- 0.189 95% CI (- 0.380, 0.003), p = 0.053]. NFPP significantly reduced parent-rated conduct problems compared to TAU across scales (p values < 0.05). No significant benefits of IY over TAU were seen for parent-rated SNAP, ADHD symptoms [- 0.16 95% CI (- 0.37, 0.04), p = 0.121] or parent-rated conduct problems (p > 0.05). The cost per family of providing NFPP in the trial was significantly lower than IY (£1591 versus £2103). Although, there were no differences between NFPP and IY with regards clinical effectiveness, individually delivered NFPP cost less. However, this difference may be reduced when implemented in routine clinical practice. Clinical decisions should take into account parental preferences between delivery approaches

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Eur J Paediatr Neurol. 2017;21:e170.

ARE WE DEALING WITH ADHD CORRECTLY?

Pisón JL.

Introduction: Attention deficit hyperactivity disorder (ADHD) is the most prevalent neurodevelopmental disorder. It can be either an isolated case or associated to other neurodevelopmental disorders such as intellectual disability, autism spectrum disorder and learning disorders. Like the other neurodevelopmental disorders it can be a manifestation of multiple neurological diseases, hereditary or acquired, such as cerebral tumours, traumatic brain injury, or Duchenne disease. The cases of children over six years old that were attended at the neuropediatric unit over a 13-month period are reviewed here, and the cases with ADHD are analyzed.

Results: Between September 2015 and October 2016, 2406 children born before the 31-08-10 were attended, and 948 of them were diagnosed as suffering from ADHD, which is 39,4% of the schoolage children that were followed at the neuropediatric unit. They were listed as having ADHD, 38,8% of those that were evaluated at any one time due to developmental delay (65/426 born before 31-8- 10). They were found to suffer from ADHD: 48,8% (19 out of 39) of the school-age children affected by neurofibromatosis 1, 16,1% (38/236) by cerebral palsy, 30% (3/10) by tuberous sclerosis, and 61,8% (92/149) of the school-age children by tics. And 25,11% (108/ 430) of the school-age epileptic children suffered from ADHD.

Discussion: Neuropediatricians manage too many conditions which lack effective treatment, and there is a very important premise for us: to treat the treatable. ADHD is common in a great number of children managed at neuropediatric units, and is the only neurodevelopmental disorder with effective treatment of its nuclear symptomatology. Is it not possible for a neuropediatrician to show no interest in ADHD. We are greatly responsible for its early identification and correct treatment

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Eur J Paediatr Neurol. 2017;21:e171.

ASSOCIATION BETWEEN SENSORY PROCESSING DISORDER AND DAILY FUNCTION OF CHILDREN WITH ATTENTION DEFICIT/HYPERACTIVE DISORDER AND CONTROLS.

Mimouni-Bloch A, Offek H, Rosenblum S, et al.

Objective: The aim of the present study was to find whether the prevalence of Sensory Processing Disorder (SPD) symptoms is similar among children with attention-deficit/hyperactivity disorder (ADHD) and typical controls, and whether SPD symptoms affect daily function among children with ADHD.

Methods: 77 children, aged 8-11 years (37 children with ADHD and 39 typical controls) were recruited. The Conner's Parent Rating Scalee Revised: Short Form (CPRSeR:S) was used to profile ADHD symptoms. The Short Sensory Profile (SSP) was used to measure sensory processing abilities. The Children Activity Scale for Parents (ChAS-P) was used to evaluate children's difficulties in daily function.

Results: The SSP total score of the ADHD group (142.13 ± 25.98) was significantly lower than that of the control group (180.08 Â± 11.68; t = -8.23). In the ADHD group, 65.8% of children had an abnormal SSP score indicating SPD, compared to only 2.6% in the control group (2 = 34.40, p < .001). The daily function of children with ADHD was significantly lower than in typical controls (ChAS-p mean 3.95±0.68; and 4.78, ±.36 in the ADHD and control groups, respectively) (t(75) = -6.71, p < .001). The largest differences were found in the category of activities involving executive functions (3.7 ± .79; and 4.76 ± .44). Children with ADHD and abnormal SSP scores, had a significantly lower daily functional ability than controls (p < .001). In contrast, children with ADHD but normal SSP had only marginally lower daily functional abilities than controls (p = .128). Overall, males had lower mean ChAS-P scores than females, however the differences were statistically-significant only among the children with ADHD. An abnormal SSP score was a weightier factor in the ChAS-P performance for males than females.
Conclusion: The present study supports the importance of SPD as a possible specifier of ADHD in children that correlates with functional consequences

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Eur J Paediatr Neurol. 2017;21:e142-e143.

ATTENTION DEFICIT HYPERACTIVITY DISORDER IN PEDIATRIC PATIENTS WITH MALIGNANT HEMATOLOGIC DISEASES AND EPILEPSY: EXPERIENCE AT A TERTIARY CARE HOSPITAL IN KOREA.

Han JY, Lee IG, Kim HS.

Objective: Pediatric patients with epilepsy and malignant hematologic diseases (MHD) are at increased risk of mental health problems compared to the general population. The purpose of this study is to identify the prevalence of attention-deficit hyperactivity disorders (ADHD) among pediatric patients treated for MHD and epilepsy in Korea.
Methods: We retrospectively reviewed 184 patients diagnosed with epilepsy and 172 patients diagnosed with malignant hematologic diseases in pediatric departments of Seoul St. Mary's hospital from May 2009 to May 2013. Normal controls were selected at out- patient clinic where they visited for vaccination.
Results: Pediatric patients with epilepsy and MHD exhibited a significantly higher rate of ADHD (29.6%, and 37.5%, respectively) compare to the controls (11.9%) (P=0.039). All groups were predominantly inattentive subtypes of ADHD. There were no significant group difference for sex and age.
Conclusion: Pediatric patients with MHD and epilepsy are at significant risk for ADHD and there is a need for efficacious intervention of ADHD. Baseline testing of all MHC and epilepsy patients is necessary to check neuropsychological and academic skills over time, in order to facilitate early intervention and prevent academic failure

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Eur J Paediatr Neurol. 2017;21:e4.

NEUROPSYCHIATRIC DISORDERS AND PSYCHOPATHOLOGY OF CHILDREN AND ADOLESCENTS WITH TUBEROUS SCLEROSIS.

Toldo I, Brasson V, Miscioscia M, et al.

Objective: To evaluate Tuberous Sclerosis (TS) associated neuropsychiatric disorders (TAND) and the caregiving's experience and the parenting stress in patients with TS.
Methods: A prospective study was conducted on a cohort of children and adolescents affected by TS. The following tests/questionnaires were administered: TAND-checklist (de Vries P.J. et al., 2015), CBCL, VABS, ECI, FES and PSI, Raven matrices (5-18 years). Moreover to adolescent patients (≥11 years; IQ> 70): YSR, MASC, CDI, SF-36 and TAS. Clinical and neuroradiological features were analyzed for each patient. Two neurological outcome scores (EGOS-ped and E-Chess score modified) were applied at last follow-up.
Results: 32 patients aged 1 to 19 years (mean 9.8 y) participated to the study. 87% of subjects had at least one TAND and 47% of cases had intellectual disability. TAND Checklist interview revealed internalizing problems in 65% of cases (vs 42% of cases found by CBCL) and externalizing problems in 84% of cases (vs 10% of cases found by CBCL). VABS results correlated with age at TS diagnosis, number of brain tubers

and ratings to EGOS-PED and E-Chess score. 39% of mothers and 31% of fathers reported difficult parent-child interaction.
Conclusions: We found the TAND-Checklist was effective in the detection of psychopathology and more precise, in some aspects, than CBCL. In our sample the following TANDs prevailed: attention deficit, speech impairment, intellectual disability, difficulties at school and poor relationships with peers. Each patient had an unique neuropsychiatric profile. Genetics, family history for TS, neuroradiological features, neurological outcomes, the presence of mental retardation and the age of onset of epilepsy correlated with some TANDs. TAND-checklist and the other questionnaires could be extensively used in clinical practice and would allow an early detection of neuropsychiatric disorders and caregiving difficulties thus contributing to improve quality of life of patients and their families

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Eur J Paediatr Neurol. 2017;21:e143.

SELF-ESTEEM REINFORCEMENT STRATEGIES IN ADHD: COMPARISON BETWEEN HYPNOSIS AND ART-THERAPY.

Castelnau P, Albert G, Chabbi C, et al.

Objective: Attention-Deficit/Hyperactivity Disorder (ADHD) is a neurodevelopmental disorder characterized by hyperactivity, impulsivity and inattention. Although diagnostic tools and therapeutics are available to identify and compensate the attention deficit, ADHD patients keep with chronic low selfesteem which alter their academic outcome and quality of life throughout lifespan. We present here some results of our research program on early self-esteem rehabilitation in ADHD based on brief therapy strategies such as medical hypnosis and modern art-therapy.
Methods: 2 groups of ADHD patients (n=8) from 6 to 12 years old were compared on a 3 months period of intervention during an open randomized study. All patients included had ADHD based on ADHD RS-IV and Conners criteria and psychometric battery tests of the sustained, selective and divided attention functions. All patients were under methylphenidate therapy. One group followed 6 hypnosis sessions and the second group followed 6 art-therapy workshops. Hypnosis used tailored metaphoric tales. Art-therapy used regular paintings and modeling techniques. Subjective questionnaires and self-esteem rating scales were submitted to both parents and subjects before and after each intervention.
Results: All patients followed the sessions. From the subjective questionnaires of the parents we observed favorable changes 3 months after each of the two intervention modalities. This was not consistently confirmed from the questionnaires of the subjects whose autoevaluation sound relatively poor. Both self-esteem rating scales used in any of the 2 groups did not show significant variations.
Conclusion: Subjective questionnaires suggest that modern arttherapy and medical hypnosis provide promising opportunities to improve self-esteem of ADHD children. This pilot study requires to be reproduced in a larger population and to set more adapted rating scales. Our observations suggest that the parents should be associated to the process and that self-esteem in ADHD is not only related to the stigmatization and behavioral consequences of this severe condition

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Eur J Paediatr Neurol. 2017;21:e106.

ATTENTION DEFICIT HYPERACTIVITY DISORDER IN CHILDREN WITH EPILEPSY.

Velez-van-Meerbeke A, Echeverria CM, SaldaÃ±a LMT, et al .

Objective: To establish the prevalence of attention deficit hyperactivity disorder in epileptic children and their siblings and to evaluate the factors that explain this association.
Methods: Observational analytical study with 185 children with epilepsy and 63 siblings aged 6 - 18 years selected from different epilepsy clinics. They were evaluated on the basis of the DSM IV for ADHD checklist and the Behavioral Assessment System for Children (BASC) for parents and teachers.
Results: Prevalence of ADHD was 39.3% in children with epilepsy and 14.4% in their siblings. Combined sub-type was the most frequent in both groups. 53.3% of the patients had focal seizures and the most frequent diagnosis was partial epilepsy (67.8%); 62% of children were on antiepileptic treatment and 52% had no seizures. There was no correlation between type or frequency of seizures, epileptic syndrome, use,

type or number of drugs or persistence of seizures and the presence of ADHD. Younger patients have a higher risk of presenting the disorder compared to older children (OR = 2.02 IC 95% = 1.08 - 3.70). Some Psychiatric symptoms like anxiety, depression, behaviour disturbances, atipicality etc. are related to the presence of ADHD. In contrast, children with good performance at school and with good social abilities had less risk (OR = .382 IC 95%= .20 - .74; OR = .35 IC 95% = .14-.89).
Conclusion: There is an important association between the presence of epilepsy and attention deficit hyperactivity disorder. However, the absence of correlation with most of the variables related to the epilepsy, the presence of psychiatric comorbidities, the high prevalence of ADHD in siblings and the low risk that exists with a good academic performance or with good social skills suggests that there are other related environmental or genetic factors

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Eur J Paediatr Neurol. 2017;21:e142.

THE CLINICAL CHARACTERISTICS OF ATTENTION DEFICIT HYPERACTIVITY.

Mahajnah M, Zelnik N.

Objective: Identifying the clinical characteristics in adolescents newly diagnosed with ADHD.
Methods: Data of patients aged 7-17 years diagnosed with ADHD was collected and analyzed. The patients divided into adolescents aged 13-17 years (Group I) and children aged 7-12 years (Group II), 592 males and 231 females. Group Iconsists of 450 subjects, Group II 373 subjects.
Results: Adolescents were predominantly inattentive (63.8%), most of Group II patients had combined or hyperactive ADHD (70.8%). Learning Disorders more common in adolescents (51.2% vs. 39.7%) and treated mainly with long- acting methylphenidate, Group II patients were treated mainly with short and medium-acting methylphenidate. Newly diagnosed adolescents were less likely to exhibit behavioral comorbidities. Headache and insomnia were reported more in adolescents, stimulant rebound effect was more in younger children.
Conclusion: While the biological nature of ADHD is similar in both age groups the primary symptomatology and associated comorbidities are prone to age- dependent changes

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Eur J Paediatr Neurol. 2017;21:e171.

AUTISM SPECTRUM DISORDER (ASD) AND ATTENTION DEFICIT HYPERACTIVITY DISORDER (ADHD) IN CHILDREN AND ADOLESCENTS WITH NEUROFIBROMATOSIS TYPE 1 (NF1).

Kalyva E, Kyriazi M, Vargiami E, et al.

Objective: Literature suggests that children and adolescents with Neurofibromatosis Type 1 (NF1) present high comorbidity with Autism Spectrum Disorder (ASD) and Attention Deficit Hyperactivity Disorder (ADHD). The aim of the present study was to corroborate this claim using the appropriate assessment methods.
Methods: The participants were 33 patients, 20 girls (61%) and 13 boys (39%) who met all the criteria for NF1 and their age ranged from 2.5-15 years. They were administered the ADOSG2 in order to ascertain the diagnosis of ASD, while their parents were given the ADI-R. They were also observed and their parents filled in the Achenbach questionnaire and the KSADS-PL to diagnose for ADHD.
Results: Only 2 children (6%) fulfilled the diagnosis of ASD, which contradicts the higher percentages presented in the literature. Another 15 children (45%) were diagnosed with ADHD, matching the percentages reported in relevant studies.
Conclusion: Findings are discussed in terms of the importance of using valid psychometric tools to establish comorbidities for children and adolescents with NF1

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Eur J Paediatr Neurol. 2017;21:e170.

NEUROPSYCHOLOGICAL BATTERY FOR THE ATTENTION DEFICIT AND HYPERACTIVITY DISORDER ASSESSMENT IN SCHOOL AGED CHILDREN.

Hernández D.

Objective: Present the design of a neuropsychological battery for the detection of main cognitive deficits in school aged children with ADHD.

Methods: The neuropsychological battery created for the present study consists of 13 subtests that were designed based on the main neuropsychological deficits described in recent literature regarding ADHD in school aged children and it has been applied to 10 children and adjustments have been made in its design.

The tests are as follows: 1. Synkinetic movements (Motor overflow). 2. Gait. 3. Synchronized movements. 4. Delay aversion. 5. Reaction time (Go/No-go task). 6. Planning. 7. Working Memory. 8. Set- shifting. 9. Temporal processing. 10. Interference control. 11. Social Cognition. 12. Rapid naming. 13. Processing speed.

Results: Until now, the battery has only been applied on a small sample to make adjustments on the application parameters, because some of the subtests are automated.

Conclusion: Covering the evaluation of deficient functions in children with ADHD, the test battery is expected to make an important contribution to diagnostic evaluations, after its validation process and standardization

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Eur J Paediatr Neurol. 2017;21:e141-e142.

CORRELATION BETWEEN SLEEP DISORDERS AND ADHD IN CHILDREN WITH ABSENCE EPILEPSY: AN OBSERVATIONAL STUDY.

Duca M, Cottone C, Maltoni L, et al.

Objective: The authors investigated sleep disorders (SD) and ADHD in children with absence epilepsy (AE) and the correlation with adverse effects of antiepileptics drugs (AED).

Methods:

Inclusion criteria: age 5-16 years, epilepsy with typical absences diagnosis, normal neurological examination. Parents completed questionnaires on sleep, AED side effects, school performances, learning problems, ADHD rating scale. Results were compared to an healthy sample. Our population was then divided into 2 groups: with and without seizures at last examination. Number, gender, family and personal history for epilepsy or febrile convulsions, AED, neuropsychological tests results when available, presence of SD were analyzed. The statistical relationships between a) SD and ADHD with AED adverse effects, b) SD and ADHD symptoms, c) the variance analysis between ADHD and SD considering the presence of seizures with the adverse effects as covariate, were considered.

Results: Seventy children with absence seizures were included in the study; 59% controlled by AED. Neuropsychological evaluation was performed in 63%, in 51% identifying one or more deficient domains. 50% had ADHD clinical diagnosis, ADHD Rating scale, performed by all sample, was positive in 37%. SD were reported in 43 % of patients: 21% breath disorders, 16% insomnia, 19% parasomnia, 11% non-restoring sleep and 11% excessive sleepiness. Statistical difference for SD was found between children with epilepsy and healthy controls ($p < 0.001$), no difference in SD between subgroups with and without seizures; statistical correlation respectively of SD ($p<0.001$), and ADHD ($p=0.000$) with AD adverse effects, significative correlation between SD and ADHD ($p=0.000$).

Conclusion: SD are not rare in children with AE. ADHD symptoms may also be present. In everyday clinical practice we advise a systematic investigation of this children, using validated questionnaires, ideally at epilepsy diagnosis and before treatment. A control at 6 months would allow early detection of eventual comorbidities and appropriate adjustment of therapeutic strategies

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Eur Neuropsychopharmacol. 2017;27:S1107.

MODAFINIL FORATTENTION-DEFICIT/HYPERACTIVITY DISORDER (ADHD): AN UPDATED SYSTEMATIC REVIEW AND META-ANALYSIS.

Lowentha R, Taiar I, Soares A, et al.

Modafinil is a central actuating agent that in high doses seems to change GABA and glutamate balance leading to hypothalamus activation, prescribed originally as a wake-promoting agent. It can be used to ADHD ameliorating symptoms through the same mechanisms by which reduces sleepiness, in addition to greater tolerance to side effects. We performed a systematic review based on Cochrane group and PRISMA statement guidelines, searching for randomized controlled trials on modafinil for ADHD in MEDLINE and EMBASE databases following the recommendations of Cochrane group. For the main outcome (ADHD symptoms score), we initially calculated the standardized mean difference and the pooled standard deviation of each comparison. The Hedges' g was used as the measure of effect size. The pooled effect size was weighted by the inverse variance method and measured using the random-effects model. The rationale for using random models was based on the fact that it can rarely be assumed that all studies involved in a meta-analysis share the exact same effect size. Heterogeneity was evaluated with the I2 (> 35% for heterogeneity) and the %2 test (p<0.10 for heterogeneity). Publication bias was evaluated using the funnel plot, which displays confidence interval boundaries to assist in visualizing whether the studies are within the funnel, thus providing an estimate of publication bias. A total of six controlled trials were eligible for the statistical analysis (n = 834; mean age = 9.5 ± 0.59) [1-5]. All but one trial used placebo as comparator group. One trial used methylphenidate as active comparator group. Modafinil dosage varied between 175-300mg daily. Every study used The Parent and Teacher ADHD Rating Scale-IV for assessing clinical symptoms. Regarding main outcome we found modafinil to be superior to comparator groups for ameliorating ADHD symptoms. Interestingly we observed a difference regarding symptoms assessment between parents and teachers dimensions (teachers: Hedgs'g = 1.06 95%CI 0.45-1.68; parents: Hedgs'g = 0.46 95% CI 0-0.86). We also found high heterogeneity between studies, following possibly the lack of a standardized study protocol. Finally, considering the effect of possible cof ounders in the effect of modafinil for ADHD symptoms, we performed multiple regressions focused on clinical and demographical variables as modafinil dosage, number of patients, use of placebo, age. We found no variable to influence the polled effect size. Albeit our positive results, some limitations should be addressed as (a) the need for adequately establishing primary outcomes given that discrepant ratings may occur between parents and teachers following subjective issues (9); (b) the need for determining more homogeneous study protocols as to guarantee results generalizability, (c) the need for rigorous heterogeneity assessment and (d) the urge for adequately reporting the results based on diferent clinical dimentions such as impulsivity, attention and hyperactivity. We found that modafinil is superior to comparator groups in the treatment of ADHD. However, given the relatively small number of trials available up-to-date further trials assessing longer follow-ups and larger samples are fundamental for clarify the precise impact of modafinil in the treatment of ADHD in daily clinical practice

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Eur Neuropsychopharmacol. 2017;27:S1114.

EFFICACY OF GUANFACINE EXTENDED RELEASE IN CHILDREN AND ADOLESCENTS WITH ADHD AND COMORBID OPPOSITIONAL DEFIANT DISORDER.

Huss M, Newcorn J, Connor D, et al.

Introduction: Individuals with attention-deficit/hyperactivity disorder (ADHD) of ten have comorbid oppositional defiant disorder (ODD), which is characterized by symptoms of anger, hostility, irritability, and refusing to comply with rules. Comorbid ODD is associated with greater ADHD symptom severity and may affect response to ADHD treatment.

Aim: The objective of these post hoc analyses was to assess the efficacy of the non-stimulant guanfacine extended release (GXR) on core ADHD symptoms in children (aged 6 and 12 years) and adolescents (aged 13 and 17 years) with and without a diagnosis of comorbid ODD using data from four phase 3 trials of GXR.

Methods: Data for this subgroup analysis were derived from four randomized, placebo-controlled trials assessing the efficacy of dose-optimized GXR monotherapy in which greater than 10% of patients had a past or current diagnosis of comorbid ODD. SPD503-312 and SPD503-316 were 10-13-week studies of GXR (1 and 7 mg/day) in children (SPD503-316) and adolescents (SPD503-312 and SPD503-316) with ADHD [1,

2]. SPD503-314 and SPD503-307 were 8-week studies of GXR (1 and 4 mg/day) in children. In SPD503-307 participants were required to have a score of 12 (females) or 14 (males) on the oppositional subscale of the Conners' Parent Rating Scale-Revised: Long Form. Efficacy was determined based on placebo-adjusted least squares (LS) mean change from baseline to endpoint (based on the last observation carried forward) in ADHD Rating Scale IV (ADHD-RS-IV) total score. LS mean change, effect size (ES) and p value were based on type III sum of squares from an analysis of covariance model.
Results: In pooled analyses of SPD503-312 and SPD503-316, 77/537 participants had a diagnosis of comorbid ODD. Placebo-adjusted LS mean (95% confidence interval [CI]) changes from baseline to endpoint in ADHD-RS-IV total score were significant in both participants with ODD (-8.6 [-14.4,-2.8]; ES 0.688; p = 0.004), and without ODD (-7.3 [-9.5,-5.0]; ES 0.598; p < 0.001). In SPD503-314, in which 73/333 participants had comorbid ODD, significant placebo-adjusted LS mean (95% CI) changes from baseline to endpoint in ADHD-RS-IV total score were observed in both participants with ODD (-12.6 [-19.6,-5.7]; ES 0.876; p < 0.001) and without ODD (-8.7 [-11.8,-5.5]; ES 0.729; p < 0.001). In SPD503-307 which included the highest proportion of participants with ODD (143/214), placebo-adjusted LS mean (95% CI) changes from baseline to endpoint in ADHD-RS-IV total score were significant in both participants with ODD (-12.7 [-17.3,-8.1]; ES 0.962; p < 0.001) and without ODD (-11.8 [-19.3,-4.4]; ES 0.842; p = 0.002).
Conclusions: In these post hoc analyses, GXR significantly reduced core symptoms of ADHD in children and adolescents with and without comorbid ODD. These findings suggest that GXR may be a suitable treatment option for children and adolescents with ADHD and comorbid ODD

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Eur Neuropsychopharmacol. 2017;27:S535.

CIRCADIAN RHYTHM AND SLEEP IN ADHD-CAUSE OR LIFE STYLE FACTOR?

Kooij S.

ADHD in children and adults is very of ten accompanied by sleep problems, that generally lead to sleepiness during the day and impaired attentiveness. The resulting sleep debt in the long term is associated with general health problems like obesity, diabetes, cardiovascular disease and cancer. During this presentation, an overview of the literature on sleep in ADHD will be discussed, as well as recent research on circadian rhythm disturbances in ADHD and its possible consequences for health in general. Sleep disorders most found in ADHD are restless leggs syndrome, sleep apnea, and the circadian rhythm sleep disorder: delayed sleep phase syndrome. In 75% of ADHD patients the sleep phase is delayed, as has been shown using melatonin measurements in saliva in children and adults, and by actigraphy measurements of movement patterns. Also body core temperature, that reflects melatonin levels at night, is delayed and slightly decreased. A late sleep pattern is of ten genetically driven, starts in childhood, and may have several consequences for health in general in the long term, which outcome is increasingly studied in ADHD patients. As ADHD and circadian rhythm sleep disorders are intertwined in the majority of cases, the question arises whether disturbed sleep may drive ADHD symptoms, or whether ADHD induces sleep problems. Also the question whether late sleep is just a matter of lifestyle will be discussed. Available evidence for treatment of late sleep with sleep hygiene, melatonin at night and bright light therapy in the morning will be discussed

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Eur Neuropsychopharmacol. 2017;27:S748-S749.

AGE-RELATED PHARMACOTHERAPY OF ATTENTION DEFICIT HYPERACTIVITY DISORDER IN ADULTS IN SLOVENIA FROM 2003 TO 2015: A POPULATION-BASED STUDY.

Stuhec M, Locatelli I.

Background: Attention Deficit Hyperactivity Disorder (ADHD) is one of the most frequent mental disorders in children and adolescents and adults, with the worldwide-pooled prevalence of 3.4% (95% CI 2.6-4.5), while the adult ADHD prevalence is estimated at 2.5-5% [1, 2]. In most European countries there is no data on age-related pharmacotherapy for Attention Deficit Hyperactivity Disorder (ADHD) medicines in adults. In adults with ADHD, a pharmacotherapy is first line treatment and the percentage of treated patients shows quality of treatment of adults with ADHD.

Aims: The main aim of this research was to obtain the data on age-related ADHD medicine treatment in adults, from 2003 to 2015 in Slovenia. The second aim was to get insight into the treatment patterns of ADHD in adults until 2015, where very few data has been available in this part of Europe, although medications are used for more than 20 years.
Method: A prescription per patient was obtained for study period (2003-2015). The national consumption was obtained from database of the Health Insurance Institute of Slovenia. Outcomes were divided to the 3 different age categories (18-24 years, 25-49 years and over 50 years). Only immediate-release methylphenidate (IR-MPH), methylphenidate-osmotic release oral delivery system (OROS-MPH) and atomoxetine (ATX) were available and included in this study. The study subjects were limited to those older than 18 years, as this study was focused on ADHD in adults. The absolute number of patients at least one prescription of ADHD medicine in each year during the study period (2003-2015) was obtained.
Results: In the age category 18-24 years, 16 patients (0.8 per 10, 000 persons aged 18-24) were treated with MPH in 2003, 130 (8.9 per 10, 000 persons) in 2015. In the other two age categories, the increase number of patients treated with MPH was not as substantial. In the age category 18-24 years, 16 patients (0.8 per 10, 000 persons aged 18-24) were treated with MPH in 2003, 130 (8.9 per 10, 000 persons) in 2015. In the age category 18-24 years the total number of patients treated with ATX was 106 (7.3 per 10, 000 persons) in 2015. In the age category 25-49 years the total number of patients treated with ATX was 158 (2.2 per 10, 000 persons) in 2015, which is higher than the number of patients treated with MPH. In the age category 50+, less only 30 patients (0.4 per 10, 000 persons) were treated with ADHD medicines.
Conclusions: Prescription rates of ADHD medications have increased dramatically in the past two years due to the approved ATX for adults ADHD. High percentage of treated ADHD patients with ATX can also be connected with a lack of approved medications for stimulants with ADHD in Slovenia (IR-MPH, OROS-MPH), low respect to the treatment guidelines and gaps in the treatment between childhood and adulthood. This is a first study in this part of Europe and therefore results could be widely use

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Eur Neuropsychopharmacol. 2017;27:S1108-S1109.

METHYLPHENIDATE LONG-TERM EFFECTS ON PSYCHIATRIC OUTCOMES IN A SARDINIAN ADHD POPULATION: PRELIMINARY RESULTS FROM THE PROSPECTIVE ADDUCE PROJECT.

Sanna E, Carucci S, Romaniello R, et al.

Background: Methylphenidate (MPH) is the most common first-line therapy for ADHD (Attention Deficit Hyperactivity Disorder) in Europe: many studies have examined its effectiveness and have shown a response rate of around 70%, with improvements seen in many areas (inattentiveness, impulsiveness and self-esteem), though its long term safety is still controversial. The Attention Deficit Hyperactivity Disorder Drugs Use Chronic Effects (ADDUCE) project is an EU funded programme to evaluate the safety of MPH in the long term by systematic review of published information, data-mining from available databases and a large multi-national prospective study (WP 3). Using the Sardinian sample of the WP 3 ADDUCE sample we investigated the association between MPH and increased risk for psychiatric adverse effects after at least 1 year of treatment.
Objectives: To evaluate, within the prospective, longitudinal, pharmacovigilance, EU funded project ADDUCE, whether methylphenidate for ADHD is associated with a statistically significant increase in long-term risk of psychiatric effects (mood disorder, suicidal behaviour, psychotic symptoms and substance misuse). We further evaluated if the onset of psychiatric adverse effects correlate to the severity of ADHD and if the MPH use in the long term interferes on tic severity.
Methods: According to the ADDUCE protocol [2], psychiatric symptoms were assessed every six months for two consecutive years by the following scales: Mood and Feelings Questionnaire (MFQ) Short Version for child and parent; Psychosis Like Symptoms (PLikS); Columbia-Suicide Severity Rating Scale (C-SSRS); Substance Use Questionnaire (SUQ).
Results: One hundred and twenty-one ADHD Sardinian subjects (104 M; 17 F), aged 6-17, were enrolled and divided into two the following groups: 66 ADHD starting on MPH for the first time (ADHD-MPH+) and 55 untreated ADHD (ADHD-NO MPH). The two groups appeared to be comparable for ADHD subtype, cognitive functioning, age and gender distribution. A significative difference between the two groups was found for ADHD symptoms severity ($p = 0.001$) and the rate of comorbidities, particularly in relation to Oppositional

Defiant Disorder (ODD; p <.001). Data from MFQ-child version, SUQ, Pliks, C-SSRS, have been analysed at two time points: baseline visit and after 24 months. 81 subjects (51 ADHD-MPH+ and 30 ADHD-NO MPH) completed the psychiatric assessment at 24 months visit. After 24 months we found a clinical trend for improvement on depressive symptoms measured by the MFQ-child version in both groups (p = 0.001 for ADHD-MPH+ and 0.007 for ADHD-NO MPH) and by the MFQ-parent version for the medicated group (p = 0.04). No significant differences were found for substance misuse, psychotic symptoms suicidal ideation and severity of tic after 24 months of treatment in the medicated group, resulting substantially comparable to the non medicated sample.
Discussion: Preliminary analysis on the present sample revealed that MPH is safe in the long term and could even help in managing depressive symptoms in the ADHD population improving the global functioning of patients. Firm conclusions on the efficacy and safety of medication on the psychiatric comorbid symptoms could be however drawn only when the total ADDUCE sample will be included in the analysis

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Eur Neuropsychopharmacol. 2017;27:S639-S640.

EFFECT OF A SINGLE DOSE OF METHYLPHENIDATE ON COGNITION IN ADULTS WITH ATTENTION DEFICIT HYPERACTIVITY DISORDERS AND PREDICTIVE THERAPEUTIC RESPONSE.

Ertle S, Vanoli L, Erb A, et al.

Background: Attention deficit/hyperactivity disorder (ADHD) affects about 60% of adults who suffered from ADHD in childhood. Symptoms in adult patients are quite different from those observed in children and the most remarkable symptoms are organization and planning difficulties, procrastination, thought lessness, memory troubles, emotional disorders and other functional impairments. Different studies have shown deficits in executive functions (for instance working memory, inhibition control, planning), memory and attentional components such as deficit of vigilance, distractibility and selective, divided or sustained attention. In child and adolescent psychiatry, methylphenidate (MPH) is the most common worldwide licensed treatment of ADHD. In different countries it is also licensed for the treatment in adult patients but in the France it is still considered as an of f-label treatment. Few studies regarding the effect of MPH in adult ADHD patients have been published during the past years compared to the children.
Objectives: The aim of this study was to assess the neuropsychological effects of a single 10 mg dose of methylphenidate on different attention components and on executive functions (working memory, inhibition, flexibility) by using the computerized Attention Assessment Battery (TAP 2.3). Self-rating visual analogical scales of Bond and Lader (subjective assess ment) were used. We also analysed if acute effects of atest dose of MPH on cognitive parameters may predict long-term outcomes with MPH medication. Methods: 97 DSM IVand DIVA 2.0-ADHD adult patients (56 males, 41 females; mean age±SD: 32.3 ± 10.8 years) were enrolled into this study. Scales such as ASRS, CAARS and WURS-25 (retrospective ADHD symptoms in childhood) were used. Neuropsychological evaluations were performed in the morning by using the TAP battery at baseline (Day 0), then 1 hour after administration of MPH (10 mg orally on day 15; i.e. MPH test), and 6 months after chronic MPH treatment with an adequate dose (mean dose ± SD/d: 46.7 ± 23.8 mg).
Results: Compared with baseline, a single dose of MPH resulted in a statistically significant improvement in working memory performance, visual scanning, phasic and selective attention, sustained attention as well as executive functions in terms of number of mistakes and omissions (all p < 0.0004). Reaction times also significantly decreased in most of these tasks (p < 0.005). Statistically significant effects (p < 0.001) were also observed regarding the subjective assessments (patients felt more alert and calmer). These improvements on cognitive functions and subjective feelings were still observed after 6 months of MPH treatment. Positive impacts on everyday life were noticed regarding the ASRS and CAARS scales compared to the baseline.
Conclusions: Adults with ADHD showed significant neuro-cognitive improvements after a single 10 mg dose of methylphenidate. This benefit on cognitive functions was still observed 6 months after chronic MPH treatment. Our results suggest that the MPH test would be useful in predicting subsequent responses to methylphenidate in ADHD adult patients

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Eur Neuropsychopharmacol. 2017;27:S1102-S1103.

EEG THETA/BETA RATIO CORRELATES POSITIVELY WITH INATTENTION AND MEMORY PROBLEMS IN ADHD AND CONTROLS.

Kiiski H, Bennett M, Kelly C, et al.

Background: Attention-deficit/hyperactivity disorder (ADHD) affects 5% adults worldwide, has diverse symptoms and little is known about its heritability. Brain electrical activity at rest, measured by electroencephalography (EEG), may shed light to the pathophysiology associated with ADHD and its heritability. Research into the electrophysiological characteristics of ADHD in adolescents has suggested that power in theta/beta ratio may be increased in ADHD in comparison to healthy participants. Recent meta-analysis reported increased slow-wave (theta) activity to be characteristic of ADHD samples relative to individuals with other externalizing behaviours. ADHD symptoms, inattention in particular, has been shown to be positively associated with theta band power [4]. However, less is known about the neurophysiological basis of adult ADHD and its association with ADHD symptoms, and whether non-affected first-degree relatives of adults with ADHD share similar electrophysiological patterns.

Objective: To investigate whether absolute and relative power in EEG frequency bands of delta, theta, alpha, beta and gamma, and in the theta-beta ratio, (a) differ among ADHD participants, unaffected siblings of people with ADHD, and healthy controls; and (b) are related to Conners' Adult ADHD Rating Scales (CAARS) subscale scores.

Methods: Resting-state, 64-channel EEG was recorded during 3-minute eyes-closed (EC) and 3-minute eyes-open (EO) conditions from 31 participants diagnosed with ADHD (mean age = 26.6, SD = 9.2), 12 unaffected siblings (mean age = 23.0, SD = 4.0) and 20 healthy controls (mean age = 24.9, SD = 6.1). They also completed CAARS questionnaire. Spectral analysis of absolute (iV2) and relative power (%) was performed for five frequency bands: delta (1-4 Hz), theta (4-8 Hz), alpha (8-13 Hz), beta (13-30) and gamma (30-80 Hz), and for the theta/beta ratio, for each of the 64 channels. Principal component analysis was conducted on each of the frequency bands and ratios, and a factor explaining most variance was extracted for each. These factors were then compared between the groups, and correlated with the CAARS subscale scores.

Results: Absolute and relative power in EC theta/beta ratio correlated positively with CAARS subscale measuring inattention and memory problems ($r = 0.37$, $p < 0.05$) over fronto-central areas in a sample of ADHD and control participants. Furthermore, in the same sample absolute and relative theta power at EC frontal and parietal locations correlated positively with CAARS's hyperactivity-restlessness score ($r = 0.40$, $p < 0.01$) and impulsivity/emotional lability score ($r = 0.35$, $p < 0.05$), and EC gamma power correlated with CAARS's problems with self-concept subscale score over widespread scalp regions. In a sample of all the participants, CAARS problems with self-concept subscale correlated positively with EC gamma band power over frontal and parietal areas ($r = 0.34$, $p < 0.01$). There were no group differences in power between the participant groups.

Conclusion: ADHD symptoms in adults are associated with neurophysiological activations as measured by the power in theta/beta ratio, and of theta and gamma bands. However, this pattern was not seen in unaffected siblings and the participant groups did not differ. Thus, electrophysiological resting state measures may have some utility as a prognostic marker for ADHD symptomology

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Eur Neuropsychopharmacol. 2017;27:S1120-S1121.

COGNITIVE CHARACTERIZATION OF OF FSPRING OF PATIENTS WITH SCHIZOPHRENIA, BIPOLAR DISORDER AND A COMMUNITY CONTROL WITH ADHD TRAITS.

Rodrguez-Toscano E, Sarabia A, Daz-Caneja CM, et al .

Background: Of fspring of patients with diagnose of Schizophrenia (SzOf f) or Bipolar Disorder (BDOf f) are con sidered a high-risk population of developing psychopathological symptoms. Compared to of fspring of healthy controls (CcOf f), SzOf f and BDOf f have shown (1) cognitive and clinical abnormalities and (2) a higher probability to develop Attention Deficit Hyper-activity Disorder (ADHD). Furthermore, characteristics of ADHD symptomatology have been suggested as early markers of a more severe psychopathology developmental course, wherein nonspecific symptoms in children progress toward a more severe, specific diagnosis in adolescence. Therefore, studying the cognitive prof ile of SzOf f and BDOf f with ADHD

symptomatology might serve to detect prodromal markers in vulnerable populations. The current study compares the cognitive profiles of three samples of SzOf f with ADHD symptoms, a sample of BDOf f with ADHD symptoms and a sample of CcOf f in with ADHD symptoms.
Methods: Twenty-four SzOf f (mean age =10, 17% female), 25 BDOf f (mean age = 12.84, 8% female) and 25 CcOf f (mean age = 11.04, 56% female) participants with ADHD symptoms (Kiddie Schedule for Affective Disorders and Schizophrenia-Present and Lifetime version scores = 2 as subthreshold diagnosis or 3 as presence of diagnose) were recruited as part of the project Bipolar and Schizophrenia Young Of fspring (BASYS), a Spanish two site naturalistic study. A broad neuropsychological battery was used to assess six cognitive domains: attention, processing speed, working memory, memory and learning, executive functioning and visual memory. Additionally, a global cognition score was computed by averaging the z-scores from each test. ANCOVAs were used for testing the main effect of group (CcOf f, SzOf f and BDOf f) on each cognitive domain and the global score, controlling for the effect of age, sex and ADHD diagnose and the variable family was randomized to control for the effect of including siblings of the same family using a mixed model. Bonferroni's method was employed to correct for multiple comparisons ($p < 0.005$).
Results: There was a significant group effect on global cognition ($F2, 68 = 8.09$, $p = 0.001$), and on two specific domains: working memory ($F2, 71 = 7.74$, $p = 0.001$) and visual memory ($F2, 73 = 4.48$, $p = 0.015$). Pairwise comparisons revealed thatSzOf f showed lower scores than both CcOf f [(d Global Cognition = 0.794, $p = 0.004$), (d Working Memory = 0.916, $p= 0.009$), (d Visual Memory = 0.688, $p = 0.045$)] and BDOf f [(d Global Cognition = 0.922, $p = 0.002$), (d Working Memory = 1.051, $p = 0.001$), (d Visual Memory = 0.686, $p = 0.026$)]. There were not significant differences between CcOf f and BDOf f.
Conclusions: The group of SzOf f with ADHD symptoms have a remarkably lower global cognitive performance compared with CcOf f and BDOf f. In SzOf f are specially altered working memory and visual memory. Our results suggest that ADHD symptoms might increase the vulnerability for other clinically relevant characteristics, such as high-order cognitive capacity

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Eur Neuropsychopharmacol. 2017;27:S1113.

TESTING THE EFFICACY OF A SMARTPHONE APPLICATION IN IMPROVING MEDICATION ADHERENCE AMONG CHILDREN WITH ADHD.

Weisman O, Schonherz Y, Harel T, et al.

Introduction: Adherence to medication is a key factor for successful treatment of children with ADHD. Studies suggest that the majority of children with ADHD are treated by primary care providers. Unfortunately, the quality of ADHD care, such as frequency of follow-up meetings is of ten poor. It was claimed that most children have no contact with their physician during the first month of pharmacotherapy. A mobile health (mHealth) approach seems viable in this respect as it may bridge the gap between physicians and patients, allowing for more frequent communications as well as better monitoring of adherence to the prescribed treatment.
Aims: The current study sought to test the utility of a new mobile application (i.e., mobile app) in promoting adherence to stimulant medications among children with ADHD. We hypo the sized that children whose parents are of fered to engage with the app (the study group) will demonstrate better adherence to drug regimen and improvement in clinical symptoms compared to children treated as usual, without the app (control group).
Methods & Statistical Analysis: The study sample included 39 children (27 males, 12 females) aged 9.56 ±2.41 years (range, 6-16 y), who met criteria for a diagnosis of ADHD according to DSM-5. Participants were randomly assigned to the study group or to the control group. Clinical assessment was conducted at baseline, week 4, and week 8, using the Clinician Rating Scale (CRS), ADHD Rating Scale (ADHD-RS), and Clinical Global Impression (CGI) scale. Drug accountability (i.e., pill counts) was recorded by parents and calculated by a clinician at week 4 and week 8. Statistical analysis was conducted with SPSS. Repeated-measures analysis of variance (ANOVA) was computed to examine the effect of the app on pill counts and symptoms severity for each of the study visits. Visits/time was treated as the within-subject variable and group identity treated as the between-subject variable. Pill-counts, CRS score, ADHD-RS score, and CGI-Severity score were handled as dependent variables.

Results: The distribution of ADHD sub-types among the 39 subjects were: combined presentation (n= 18), inattentive presentation (n = 16), hyperactive/impulsive presentation (n = 4), and ADHD-NOS (n=1), with no significant difference between groups, $p > 0.05$. Notably, Participants who were prescribed with the app demonstrated higher overall medication adherence over 8-weeks period, $F = 4.33$, $p<0.05$, $r2 = 0.12$. In addition, a significant improvement in total CRS score was found among the study group in week 4 and week 8 as compared to the control group, $F = 4.74$, $p < 0.05$, $r2 = 0.13$.
Conclusions: The current findings provide initial support for the utility of mobile interventions geared toward the promotion of adherence to pharmacotherapy treatment in psychiatric populations, specifically, among youth with ADHD

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Eur Neuropsychopharmacol. 2017;27:S1109-S1110.

A RANDOMIZED, DOUBLE BLIND, PLACEBO-CONTROLLED, EFFICACY STUDY OF OMEGA 3/6 IN CHILDREN WITH MILD TO MODERATE INATTENTIVE ADHD-PRELIMINARY RESULTS.

Carucci S, Romaniello R, Masi G, et al.

Background: Attention Deficit Hyperactivity Disorder (ADHD) is a child psychiatric disorder characterized by inattention, hyperactivity and impulsivity with a significant global functional impairment. Treatment is based on behavioural and pharmacological approaches. Recently there has been a growing interest in nonpharmacological treatments, as dietary supplementation of omega-3/6 fatty acids, which seem to be deficient in ADHD individuals and moderately effective in reducing inattentive symptoms.
Objectives: The primary objective was to evaluate the efficacy of a specific Omega-3/6 combination dietary supplement in a population of Italian children with predominantly Inattentive Type of ADHD (ADHD-I). The primary efficacy measure was the change from baseline of the ADHD Rating Scale (ADHD-RS-IV) score. The secondary objectives were to evaluate the efficacy of Omega3/6 supplement compared to placebo on global functioning and severity of illness by using respectively the Children-Global Assessment Scale (C-GAS), the Clinical Global Impression of Improvement (CGI-I) and the Clinical Global Impression-Severity (CGI-S). Depression and anxiety symptoms were also assessed by the CDRS-R (Children's Depression Rating Scale-Revised) and MASC (Multidimensional Anxiety Scale for Children).
Methods: The study was a randomised, double-blind, multicentre, placebo-controlled efficacy trial of Omega-3/6 combination in children aged 6 and 12 with mild to moderate ADHD-I, according to DSM-IV criteria. The study, conducted in 4 Italian sites (Cagliari, Roma, Pisa and Messina), included a screening and baseline assessment, a phase I double blind evaluation of Omega-3/6 supplement vs placebo (6 months) and a phase II open label treatment period of further 6 months during which all subject were on the Omega3/6 dietary supplement. Clinical assessments have been performed at 5 time points: baseline, 1 month, 3 months, 6 months and 12 months.
Results: 160 drug nave ADHD Italian children (118 M; 42 F) were enrolled. 45 patients did not complete the study (drop out 28%). Preliminary results have been obtained by analysing scores at baseline visit and after 12 months. By this way, we included in the analysis both patients treated with active supplement for 12 months and patients treated openly with Omega3/6 supplement only for the last six months. Statistical significance was calculated by ANOVA for repeated measures. A significant effect at the end of the study ($p < 0.001$) was found for the following scales: ADHD-RS total score, ADHD-RS-Inattentive, CGI-S, CGI-I, CGAS. No significant changes were found for ADHD-RS-Hyperactivity and CDRS. Further analysis are in due course.
Discussion: Preliminary results suggest a significant improve ment in global functioning and in ADHD symptoms severity, after at least 6 months of treatment with Omega-3/6 dietary supple mentation. Omega-3/6 fatty acids resulted significantly effective especially in reducing the inattention symptoms. Considering the limited choice of interventions for treatment in ADHD-I children, Omega-3/6 supplementation may of fer a natural intervention to improve the quality of life of this population

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Eur Neuropsychopharmacol. 2017;27:S1095-S1096.

THE IMPACT OF ATTENTION DEFICIT HYPERACTIVITY SYMPTOMS ON MINDFULNESS.

Goksan YB, Onal SA, Yavuz M.

Introduction: Mindfulness which has its roots in Buddhist philosophy involves concentrated attention to present experience. Mindfulness involves self-regulation of attention to the experience of the present moment and decentered, non-judgmental awareness, referring to openness to one's internal and external experiences. Mindfulness has been found to be affected by emotional states. A better understanding of what factors are associated with mindfulness would be useful in exploring the efficacy of mindfulness-based therapies.

Aim: We hypothesized that besides depressive, anxiety and stress levels, attention deficit hyperactivity disorder (ADHD) symptoms would negatively correlate with the level of mindful ness since attention has the primary role in both ADHD and mindfulness.

Method: Seventy-six subjects who applied to the outpatient unit Acibadem Maslak Hospital, Psychiatry Department, Istanbul, Turkey for the first time participated in this cross-sectional study. The control group consisted of 32 healthy gender and age matched participants. Mindful Attention Awareness Scale, Depression Anxiety Stress Scale, Adult ADHD Self-Report Scale (ASRS v1.1), Wender Utah Rating Scale were given to the participants. Frequencies and descriptive statistics were calculated for all study variables. Variables were checked for normality variance. Independent t test was used to compare the means scores between groups. Categorical data was analyzed by chi-square analysis. In order to explore whether ADHD symptoms, depression, anxiety, stress, age and sex were related to mindfulness levels, linear regression analyses were used with MAAS as the dependent. Bivariate correlations were computed to examine the relationship between the variables A probability level of $p < 0.05$ was used to indicate statistical significance.

Results: DASS depression, anxiety and stress scores were significantly higher in the study group compared to the control group (16.45 ± 9.11 vs. 3.97 ± 4.40, p ‰ 0.001; 13.55 ± 7.81 vs. 3.59 ± 3.26, p ‰ 0.001; 20.41 ± 8.27 vs. 8.06 ± 4.73, p ‰ 0.001; respectively). MAAS total scores were significantly lower in the study group compared to the control group (52.29 ± 13.25 vs. 68.81 ± 11.94, p ‰ 0.001). ASRS attention subscores, hyperactivity subscores, and total scores were significantly higher in the study group compared to the control group (17.63 ± 6.71 vs. 8.28± 4.72, ‰ 0.001; 16.26 ± 5.96 vs. 9.09 ± 4.62, p ‰ 0.001; 33.89 ± 11.24 vs. 17.38 ± 8.11, ‰ 0.001, respectively). WURS results showed significant difference between study group and control group (31.33 ± 17.68 vs. 13.29 ± 7.6, p ‰ 0.001). In the linear regression model, WURS (p ‰ 0.001), DASS depression subscale (p = 0.004), ASRS attention subscale scores (p = 0.01) were found as significant predictors when MAAS score was a dependent variable. Higher depression, anxiety, and stress levels were significantly associated with lower mindfulness (r =-0.288, p = 0.012; r =-0.324, p = 0.004; r =-0.317, p = 0.005; respectively). In addition higher scores on the ASRS attention subscale, hyper-activity/impulsivity subscale, ASRS total and WURS scores also revealed lower mindfulness in the study group (r =-0.543, p ‰ 0.001; r =-0.387, p = 0.001; r =-0.516, p ‰ 0.001; r =-0.560, p ‰ 0.001; respectively).

Conclusion: Our findings showed that childhood ADHD symptoms, depression levels, and adult attention deficit symptoms significantly predicted low levels of mindfulness. Our findings demonstrated that besides emotional symptoms such as depression, anxiety and stress, ADHD symptoms also had a significantly negative impact on mindfulness. Therefore improving mindful-ness through practice of fers a novel approach in the multimodal treatment of ADHD

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Eur Neuropsychopharmacol. 2017;27:S1111-S1112.

ENDURING EFFECTS OF METHYLPHENIDATE ON SLEEP IN CHILDREN WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER: A DOUBLE-BLIND RANDOMIZED CONTROLLED TRIAL.

Solleveld MM, Schrantee A, Baek HK, et al.

Background: Methylphenidate (MPH), the most commonly prescribed stimulant for Attention Deficit Hyperactivity Disorder (ADHD), effectively improves behavioral symptoms of ADHD. However, possible (side) effects of MPH on sleep have not been well studied. The question whether or not ADHD medications affect sleep poses a serious concern for parents and psychiatrists, also because preclinical studies suggest that exposure to ADHD medications during brain development can induce long-lasting changes. The aim of the current study was therefore twof old. Our first aim was to investigate the effects of MPH on sleep in

medication-naive children for a relatively long treatment period of 16 weeks. Our second aim was to investigate whether the effects of MPH on sleep would outlast the pharmacological clearance of MPH. Based on the available literature, we hypothesized a negative effect of MPH on sleep, that would persist after treatment cessation.
Methods: In a double-blind, placebo controlled randomized clinical trial (Effects of Psychotropic Drugs on Developing Brain-Methylphenidate; ePOD-MPH) 50 medication-naive boys with ADHD between 10 and 12 years of age were included. Subjects were treated for 16 weeks with either MPH or placebo. Sleep was assessed using actigraphy and a sleep diary. Sleep was assessed at three time-points: prior to randomization, during treatment (week 8) and one week after treatment discontinuation (in week 17). Our main outcome measure was sleep efficiency, which is defined as the objective total sleep time divided by the objective time in bed, multiplied by 100 (%), and is thought to best summarize the quality, composition, continuity and consolidation of sleep. Our secondary outcome measures focused on timing and duration of sleep. Linear mixed models were used to analyze the data. Covariates included melatonin use (N = 9 at all time-points) and restless legs syndrome severity scores (N = 13 above cut-off prior to randomization).
Results: A significant time x treatment interaction effect was found for actigraphically estimated sleep efficiency ($p = 0.007$). MPH significantly improved sleep efficiency at trial end compared to baseline (+4.94%; $p = 0.005$), whereas no such effect occurred in the placebo condition (+0.97%; $p = 0.868$). Furthermore, after trial end the MPH condition showed higher sleep efficiency than the placebo condition (+5.84%; $p < 0.001$). In addition, positive effects of MPH treatment were found on timing and duration of sleep, indicating that the subjects treated with MPH fell asleep earlier, had a shorter sleep onset latency, and slept longer compared to the placebo condition and/or baseline. Inclusion of the covariates did not affect the findings.
Conclusions: In this RCT involving medication-naive boys with ADHD, we found a strong, positive effect of 16 weeks MPH treatment on the timing, duration and quality of sleep in boys with ADHD. As prior studies with shorter study durations found no-, or negative effects, our results indicate that a longer treatment period is needed to properly evaluate MPH related sleep problems. Interestingly, these effects persisted at least one week after drug clearance, in line with our findings on dopamine function in these children

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Eur Neuropsychopharmacol. 2017;27:S563.

FMRI NEUROFEEDBACK IN ADHD.

Rubia K, Alegria A, Wulff M, et al.

Introduction: Right inferior frontal cortex (rIFC) is consistently underactivated in ADHD children during cognitive control and consistently upregulated with psychostimulant medication. We conducted a proof of concept randomised controlled trial (RCT) of rtfMRI-NF of rIFC in ADHD adolescents.
Methods: Thirty-one ADHD boys were randomized in a single-blind RCT to rt-fMRI-NF (14 sessions) of the rIFC (active group) or the left parahippocampal gyrus (lPHG, control group). Visual feedback was presented via a video-clip of a rocket that had to be moved to space. Main outcome measures were changes in parents' rating of clinical ADHD symptoms which were assessed at pre, post, and on average 11 month follow-up. A computer-based test battery and a fMRI Stop task were also used to assess NF effects on cognition and IFC brain function.
Results: Both groups showed significant linear progressive activation increase with increasing NF sessions in their respective target regions relative to the other group. Both groups also showed significant reduction of ADHD symptoms after treatment and at 11 month follow-up, but with no significant group differences. Only the active group, however, showed a transfer effect (increasing rIFC activation without NF), improved trend-wise in sustained attention, showed increased IFC activation during the stop task and showed significant correlations between brain activation and clinical changes.
Conclusions: The proof of concept study shows that rtfMRI-NF is a feasible neurotherapy for ADHD adolescents, that is associated with improved short and longer-term ADHD symptoms, cognitive attention and inhibitory rIFC activation

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Eur Neuropsychopharmacol. 2017;27:S1090-S1091.

EXECUTIVE FUNCTIONS, ATTENTION AND VERBAL FLUENCY OF CHILDREN WITH ATTENTION DEFICIT/HYPERACTIVITY DISORDER USING METHYLPHENIDATE.

Minervino C, Cruz LFP.

Background: Attention Deficit/Hyperactivity Disorder (ADHD) is a neurodevelopmental disorder that negatively affects the quality of life of patients and affects approximately 3-7% of school-aged children. It is characterized by the symptomatological triad of inattention, hyperactivity and impulsivity and its also related to deficits on executive functions, attention and verbal fluency. Methylphenidate is the most widely used psychostimulant in the treatment of ADHD. Considering the increase of consumption and prescription of methylphenidate and the increase of the ADHD diagnoses, the present study aimed to analyze the performance profile on executive functions (working memory, inhibitory control and cognitive flexibility), attention (sustained, selective, alternated) and verbal fluency (phonological and semantic) of children with ADHD using methylphenidate.

Methods: A total of 71 children aged 7-11 years old were divided into three groups: control group (n = 38), ADHD group with methylphenidate (n=13) and ADHD group without methylphenidate (n = 20). The parents or responsible for the children signed a Free and Informed Consent Form and completed a sociodemographic questionnaire, and parents of children with ADHD also completed the SNAP-IV The children signed the Minor Assent Term. The instruments used in order to reach the proposed objectives were Progressive Matrices of Raven, Digit Span, Corsi Block Test, Trail Making Test, Five Digit Test and Verbal Fluency Test. After tested and confirmed the homogeneity of the variance between groups ($p > 0.05$), it was decided to use ANOVA one-way and correspondence analysis.

Results: Through ANOVA one-way, it was observed there was a significant difference between the averages of the three groups for the abilities of working memory [$F (2, 68) = 5.28$; $P < 0.05$], cognitive flexibility [$F (2, 68) = 6.71$; $P < 0.05$], inhibitory control [$F (2.68) = 4.66$; $P < 0.05$], sustained attention [$F (2.68) = 4.79$; $P < 0.05$], selective attention [$F (2.68) = 5.81$; $P < 0.05$] and alternated attention [$F (2.68) = 8.16$; $P < 0.05$]. With the post hoc it was possible to verify that the difference of averages was between the control group (CG) and the ADHD with methylphenidate or between the CG and the two experimental groups, since $p < 0.05$. Observing the means of the scores obtained by the groups, it was seen that these differences were better for the CG that obtained the highest scores. Correspondence analysis were also performed and was observed an association between the use of the medication and the achievement of an average performance on cognitive flexibility, inhibitory control and selective attention.

Conclusions: The analysis indicated that children with ADHD using methylphenidate, compared with other children with the disorder who do not use medication and with healthy children, presented a lowered profile of executive and attentional function in gregarding the abilities of inhibitory control, cognitive flexibility, working memory, sustained attention, selective attention, alternated attention, phonological verbal fluency and semantic verbal fluency

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Eur Neuropsychopharmacol. 2017;27:S1097-S1098.

EXECUTIVE FUNCTIONS IN CHILDREN WITH AN ATTENTION DEFICIT HYPERACTIVITY DISORDER, PERVASIVE DEVELOPMENTAL DISORDER AND LANGUAGE SPECIFIC DISORDER.

Candon Gamez MJ, Romero Guillena SL, Regli RE.

Introduction: The construct of executive functions is defined as the cognitive processes involved in self-regulated behaviours and thoughts. A number of neurological and mental disorders are associated with an impaired executive function. Evaluating executive function requires establishing the functional and predictive relationship between test results and subject's behaviour in daily life activities (ecological validity).

Objectives: The main objective of this study was to assess executive function in pediatric patients with a diagnosis of Attention Deficit Hyperactivity Disorder (ADHD), Pervasive Developmental Disorder (PDT), and Language Specific Disorder (SLI). The secondary objective was investigating whether alterations in executive functions are predictors of future performance of the subject in daily life activities.

Methods: The study included 80 subjects (16 girls and 64 boys) treated at a Pediatric Mental Health Unit. The mean age of subjects was 9.8 years (8-12 year interval). Diagnosis was based on ICD-10 (World Health Organization), ADHD (44 subjects: 35 boys and 9 girls), PDT (23 subjects: 22 boys and 1 girl) and TEL (13

subjects: 7 boys and 6 girls). Subjects did not have any associated psychiatric comorbidities. Their intelligence quotient (IQ) was normal according to standard IQ tests. Executive functions were evaluated using the Neuropsychological Evaluation of Executive Functions in Children (ENFEN). The battery consists of four tests: verbal fluency, trails, washers and resistance to interference which assess mental flexibility, working memory, planning and response inhibition, respectively ENFEN scores will be first converted into typical scores and next they were adapted to ten scores which range from 1 and 10, where scores 1 and 4 are considered low. Subjects were asked to complete the ENFEN questionnaire during the 2012-2013 academic year. The results obtained with the individualized therapy plan designed in the Pediatric Mental Health Unit were evaluated during the first trimester of 2015. A. subject was considered to have good performance in daily life activities if at the end of the evaluation period by the Mental Health Unit the patient showed functional improvement and was discharged, or a psychopathological or behavioral improvement was observed. Student's t-test and Chi-square test were used to assess differences between gropups Statistical analysis was performed with SPSS 22.0.

Results: 70% of subjects obtained low scores on the ENFEN scale (scores 1 and 4). No significant differences were observed in ENFEN scores among the three study groups. ENFEN scores were low (scores 1 and 4) in 72% of subjects with ADHD, 68% of subjects with PDT, and 64% of subjects with TEL. At the end of follow-up, 14 subjects were discharged from the Mental Health Unit due to improvement, 10 showed a favorable evolution, and no significant changes were observed in 31 subjects. No relationship was observed between ENFEN scores (or in any of its subscales) and future performance of the patient in daily life.

Conclusions: This study shows that a high proportion of subjects had an impaired executive function, with low scores on the ENFEN scale. The results obtained in the evaluation of executive functions are not predictors of the future performance of the subject in daily life

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Eur Neuropsychopharmacol. 2017;27:S1088.

EXAMINING THE RELATIONSHIP BETWEEN ATTENTION DEFICIT HYPERACTIVITY DISORDER, BEHAVIOURAL FEATURES AND OBESITY IN TURKISH CHILDREN AND ADOLESCENTS.

Onal SA, Goksan YB, Aka S, et al.

Introduction: There is a growing number of studies which report an association between attention deficit hyperactivity disorder (ADHD) and obesity. It is important to investigate this association in different cultural backgrounds. Both the manage ment of ADHD and prevention of childhood obesity are important health issues in the field of pediatric health care.

Aim: To our knowledge, the prevalence of ADHD in obese Turkish children has not been explored. Under the highlight of the literature we hypothesized that overweight/obese children and adolescents would be at higher risk for ADHD.

Method: This is a cross-sectional study conducted in the outpatient unit of child and adolescent endocrinology department of Acibadem Maslak Hospital, Istanbul, Turkey. The sample consisted of 55 children and adolescents aged between 6-14 years with body mass index greater than 95th percentile. A non-obese, age and sex matched control group (n = 37) was recruited from general pediatric outpatient clinic of Acibadem Maslak Hospital. The parent rated Strengths and Difficulties Questionnaire and The Turgay Diagnostic and Statistical Manuel of Mental Disorders Based Child and Adolescent Behavior Disorders Screening and Rating Scale has been used. Mann Whitney U test was used to compare the means scores between groups. Categorical data was analyzed by chi-square analysis or Fisher's Exact Test, Binary logistic regression analysis was used to determine the independent predictors of being obese. Hosmer-Lemeshow goodness of fit statistic was used to assess model fit. A probability level of $p < 0.05$ was used to indicate statistical significance.

Results: According to T-DSM-IV-S, the rates of ADHD attention deficit subtype, hyperactivity/impulsivity subtype, and the combined type were higher in the obese group compared to the control group. The rates of inattentive subtype, hyperactivity/impulsivity subtype, and the combined type in the subject group were 10.9%, 3.6%, 7.3%, respectively. The rates of inattentive subtype, hyperactivity/impulsivity subtype were 5.4%, 2.7%, respectively in the non-obese group. In terms of SDQ scores, peer problems subscale scores were significantly higher in the subject group than the control group (5.13 ± 1.24 vs 4.32 ± 1.18, $p = 0.003$). When the hyperactivity/impulsivity subscale cut off score was set at 7 and above, the rate of clinically

abnormal sample was 9.4% in the subject group, and 8.3% in the control group. Even though the rate of clinical ADHD symptoms was higher in the subject group than the control group, it did not reach to a statistically significant level. The rate of abnormal peer problems was significantly higher in the obese group (37%) compared to the non-obese participants (13.5%) ($p = 0.014$). According to the binary regression analysis, having peer problems was found to be significantly related to being obese (Exp B (OR): 3.3, $p = 0.04$).

Conclusion: We have shown that obese children and adoles cents have higher rates of ADHD symptoms and problems in peer relations. Underestimation of ADHD might be a risk factor for treatment failure in obesity since ADHD symptoms cause lack of motivation and compliance [4]. Diagnosis and treatment of ADHD symptoms might lead to an improvement in eating behaviors and in BMI values

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Eur Neuropsychopharmacol. 2017;27:S1092.

UNDERSTANDING THE ROLE OF THE AMYGDALA IN ATTENTION-DEFICIT/HYPERACTIVITY DISORDER: ASSOCIATION BETWEEN BRAIN STRUCTURE, FUNCTION AND DELAY AVERSION.

Van DJ, Moerkerke M, Sonuga-Barke E, et al.

Background: Neuroimaging studies have demonstrated structural alterations in brain regions constituting part of the affective network in individuals with attention deficit/hyperactivity disorder (ADHD). The strongest effect size compared to controls was found for the amygdala, a key component of the brain circuit responsible for processing and experience of negative emotions. Functional magnetic resonance imaging (MRI) studies have associated amygdala hyper-activation as a mediating factor in delay aversion. This negative emotional experience toward delay is considered to play a crucial role in the motivation of persons with ADHD. By using voxel-based morphometry of the grey matter, we investigated the link between structural and functional neuroanatomy, and self-reported measures of delay aversion in ADHD.

Methods: Structural T1-weighted 3T MRI scans from 28 right-handed male adolescents with combined type ADHD and 32 age-matched (10-18 years) controls were analysed using Computational Anatomy Toolbox 12. Groups were compared on grey matter volumes. Volumes in regions displaying group differences (FWE-corrected $p < 0.05$) were then correlated with delay aversion self-ratings and their neural activity measured in response to delay related cues in an fMRI task. Different cue types signaled three delay related consequences: one indicated that post-response delay occurred irrespective of response speed (CERTAIN DELAY), a second that delay would follow only when participants responded to late (CONDITIONAL DELAY), a third, that no delay would be imposed regardless of response speed (NO DELAY). The anticipatory brain responses were calculated for the CERTAIN DELAY > NO DELAY contrast in Statistical Parametric Mapping 12.

Results: No total intracranial volume, nor total grey matter differences were found between both groups. Adolescents with ADHD had significantly reduced volumes of the bilateral amygdala (Cohen's d left/right side =-0.64 and-0.75), para-hippocampus (d =-0.53 and-0.61) and medial temporal gyrus extending anteriorly to the temporal pole (d =-1.00 and-1.01) compared to controls. Individuals with ADHD rated themselves as significantly ($p < 0.01$) more delay averse then controls. The amygdala volumes were significantly ($p < 0.01$) associated with the functional activity during the delay-related task (Pearson correlation left/right r =-0.35 and-0.32) and with their self-reported delay averse behaviour (r =-0.43 and-0.45).

Conclusion: Variations in amygdala structure and function are implicated in delay aversion in ADHD. Longitudinal studies are required to disentangle whether such structural alterations are a cause or an effect of delay aversion. From a clinical perspective, this association underlines how vital it is to take delay into account when trying to interpret what situations and experiences may provoke negative reactions in persons with ADHD. These negative feelings towards delay seem to occur regardless of the possibility of comorbid symptoms of emotional dysregulation in ADHD, as only 3 participants of the ADHD group showed oppositional defiant disorder comorbidity

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Eur Psychiatry. 2018;47:42-48.

THE DANGER OF BEING INATTENTIVE ADHD SYMPTOMS AND RISKY SEXUAL BEHAVIOUR IN RUSSIAN ADOLESCENTS.

Isaksson J, Stickley A, Koposov R, et al.

Background Prior research has indicated that attention-deficit/hyperactivity disorder (ADHD) symptoms may be associated with an increased likelihood of engaging in risky sexual behaviour (RSB). However, research on this association among adolescents has been comparatively limited and mainly confined to North America. The aim of this study was to examine if inattention and hyperactivity/impulsivity symptoms were linked to RSB in a community cohort sample of Russian adolescents.

Methods The study was based on a group of 537 adolescents from Northern Russia. Information on inattention and hyperactivity/impulsivity as well as conduct problems was obtained through teacher ratings, while information on RSB (previous unprotected sex, number of sexual partners, sex while intoxicated and partner pregnancies), substance use, perception of risk, and parenting behaviour was based on students self-reports. Binary logistic regression analysis was used to examine associations between the variables.

Results Teacher-rated inattention symptoms predicted RSB, independently of co-morbid conduct problems, substance use, risk perception, and different parenting styles (parental warmth, involvement and control). In addition, male sex, binge drinking and a lower assessment of perceived risk were all significantly associated with RSB in an adjusted model. Neither teacher-rated hyperactivity/impulsivity symptoms nor conduct problems were linked to RSB in the full model.

Conclusions Deficits in planning and organizing behaviours, being easily distracted and forgetful seem to be of importance for RSB in Russian adolescents. This highlights the importance of discriminating between different ADHD symptoms in adolescence to prevent risk behaviours and their potentially detrimental outcomes on health and well-being

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Front Psychiatry. 2017;8.

THE UTILITY OF A COMPUTERIZED ALGORITHM BASED ON A MULTI-DOMAIN PROFILE OF MEASURES FOR THE DIAGNOSIS OF ATTENTION DEFICIT/HYPERACTIVITY DISORDER.

Crippa A, Salvatore C, Molteni E, et al.

The current gold standard for diagnosis of attention deficit/hyperactivity disorder (ADHD) includes subjective measures, such as clinical interview, observation, and rating scales. The significant heterogeneity of ADHD symptoms represents a challenge for this assessment and could prevent an accurate diagnosis. The aim of this work was to investigate the ability of a multi-domain profile of measures, including blood fatty acid (FA) profiles, neuropsychological measures, and functional measures from near-infrared spectroscopy (fNIRS), to correctly recognize school-aged children with ADHD. To answer this question, we elaborated a supervised machine-learning method to accurately discriminate 22 children with ADHD from 22 children with typical development by means of the proposed profile of measures. To assess the performance of our classifier, we adopted a nested 10-fold cross validation, where the original dataset was split into 10 subsets of equal size, which were used repeatedly for training and testing. Each subset was used once for performance validation. Our method reached a maximum diagnostic accuracy of 81% through the combining of the predictive models trained on neuropsychological, FA profiles, and deoxygenated-hemoglobin features. With respect to the analysis of a single-domain dataset per time, the most discriminant neuropsychological features were measures of vigilance, focused and sustained attention, and cognitive flexibility; the most discriminating blood FAs were linoleic acid and the total amount of polyunsaturated fatty acids. Finally, with respect to the fNIRS data, we found a significant advantage of the deoxygenated-hemoglobin over the oxygenated-hemoglobin data in terms of predictive accuracy. These preliminary findings show the feasibility and applicability of our machine-learning method in correctly identifying children with ADHD based on multi-domain data. The present machine-learning classification approach might be helpful for supporting the clinical practice of diagnosing ADHD, even fostering a computer-aided diagnosis perspective

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Int J Neurosci. 2017;1-12.

INVESTIGATION OF ATTENTION DEFICIT HYPERACTIVITY DISORDER (ADHD) SUB-TYPES IN CHILDREN VIA EEG FREQUENCY DOMAIN ANALYSIS.

Aldemir R, Demirci E, Per H, et al.

Aim of the study: To investigate the frequency domain effects and changes in electroencephalography (EEG) signals in children diagnosed with attention deficit hyperactivity disorder (ADHD).

Patients and methods: The study contains 40 children. All children were between the ages of 7 and 12 years. Participants were classified into four groups which were ADHD (n=20), ADHD-I (ADHD-Inattentive type) (n=10), ADHD-C (ADHD-Combined type) (n=10), and control (n=20) groups. In this study, the frequency domain of EEG signals for ADHD, subtypes and control groups were analyzed and compared using Matlab software. The mean age of the ADHD children's group was 8.7 years and the control group 9.1 years.

Results: Spectral analysis of mean power (¼V2) and relative-mean power (%) was carried out for four different frequency bands: delta (0--4 Hz), theta (4--8 Hz), alpha (8--13 Hz) and beta (13--32 Hz). The ADHD and subtypes of ADHD-I, and ADHD-C groups had higher average power value of delta and theta band than that of control group. However, this is not the case for alpha and beta bands. Increases in delta/beta ratio and statistical significance were found only between ADHD-I and control group, and in delta/beta, theta/delta ratio statistical significance values were found to exist between ADHD-C and control group.

Conclusion: EEG analyzes can be used as an alternative method when ADHD subgroups are identified

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Int J Pediatr Adolesc Med. 2017.

PREVALENCE OF ATTENTION DEFICIT HYPERACTIVITY DISORDER AMONG PRIMARY SCHOOL-CHILDREN IN RIYADH, SAUDI ARABIA; 2015-2016.

Albatti TH, Alhedyan Z, Alnaeim N, et al.

Objectives: The aim of the study was to 1) determine the prevalence of Attention Deficit Hyperactivity Disorder (ADHD) among both governmental and private primary Saudi school children, 2) measure the gender difference of ADHD prevalence, and 3) determine any association between the socio-demographic characteristic of the parents of children with ADHD.

Methods: This is an observational cross-sectional study of 1000 primary school children belonging to 1st, 2nd and 3rd grade. The selected students were screened by the ADHD rating scale using multistage sampling technique. The first stage was selection of 20 schools from all Riyadh regions by simple randomization. The second stage was choosing children whom serial numbers were multiples of five in each class. The ADHD rating scale was filled by both parents and teachers along with a socio-demographic questionnaire for the parents.

Results: The estimated prevalence of ADHD was 3.4%. ADHD manifestations affect boys more than girls. In addition, ADHD was more frequent among children of illiterate mothers. Finally, ADHD was significantly more prevalent among first grade children.

Conclusion: This epidemiological study filled the data gap of ADHD prevalence in Riyadh. The study's findings go in line with many nearby and global studies

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J Adv Pharm Technol Res. 2017;8:138-42.

THE EFFECT OF ADDING FERROUS SULFATE TO METHYLPHENIDATE ON ATTENTION-DEFICIT/HYPERACTIVITY DISORDER IN CHILDREN.

Panahandeh G, Vatani B, Safavi P, et al.

Attention deficit/hyperactivity disorder (ADHD) is one of the most common psychiatric disorders in children with several complications. This study was conducted to investigate the effect of adding ferrous sulfate to methylphenidate in decreasing ADHD symptoms. This study was a double-blind, randomized clinical trial. In this study, 42 nonanemic children with ADHD and serum ferritin below 30 mg/ml were enrolled according to convenience sampling and randomly assigned to two groups of 21 each, cases and controls. The two groups

were matched for age and sex. The case group was administered with ferrous sulfate 5 mg/kg in addition to methylphenidate up to 1 mg/kg and the control group with methylphenidate alone. The scores on child symptoms inventory-4 (CSI-4) were recorded at baseline and after 2 months of treatment. Data were analyzed by t-test, Pearson's correlation coefficient, and repeated measures ANOVA in SPSS 16. The scores on CSI-4 decreased significantly at month 2 in both groups ($P < 0.001$). The scores on attention deficit and hyperactivity subscales of the CSI-4 were significantly lower in the case group than the control group ($P < 0.05$). The total score on CSI-4 decreased more markedly in the case group ($P < 0.04$). Use of ferrous sulfate plus methylphenidate can be effective in reducing ADHD symptoms in nonanemic children with low serum ferritin

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J Child Neurol. 2017;32:1083-91.

ATTENTION-DEFICIT HYPERACTIVITY DISORDER (ADHD) IN EPILEPSY AND PRIMARY ADHD: DIFFERENCES IN SYMPTOM DIMENSIONS AND QUALITY OF LIFE.

Ekinci O, Okuyaz Ã, et al.

Purpose: We aimed to (1) compare quality of life (QOL) among children with epilepsy, epilepsy and attention-deficit hyperactivity disorder (ADHD), and primary ADHD and (2) compare ADHD symptom dimensions and subtypes between children with epilepsy-ADHD and primary ADHD.

Methods: A total of 140 children; 53 with epilepsy, 35 with epilepsy-ADHD, and 52 with primary ADHD were included. KINDL-R (quality of life measure), Turgay DSM-IV Disruptive Behavior Disorders Rating Scale (T-DSM-IV-S), and Conners Parent Rating Scale (CPRS) were completed. Neurology clinic charts were reviewed for epilepsy-related variables.

Results: Children with epilepsy-ADHD had the lowest (poorest) KINDL-R total scores. Epilepsy-ADHD group had more inattentiveness symptoms, whereas primary ADHD group had more hyperactivity/impulsivity symptoms. The frequencies of ADHD combined and inattentiveness subtypes were 60% and 40% in children with epilepsy-ADHD and 80.7% and 19.3% in children with primary ADHD, respectively ($P = .034$).

Conclusion: ADHD in epilepsy is associated with a significantly poor quality of life and predominantly inattentiveness symptoms

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J Commun Disord. 2017;70:25-34.

AN EXPLORATION OF SARCASM DETECTION IN CHILDREN WITH ATTENTION HYPERACTIVITY DEFICIT DISORDER.

Ludlow AK, Chadwick E, Morey A, et al.

The present research explored the ability of children with ADHD to distinguish between sarcasm and sincerity. Twenty-two children with a clinical diagnosis of ADHD were compared with 22 age and verbal IQ matched typically developing children using the Social Inference Minimal Test from The Awareness of Social Inference Test (TASIT, McDonald, Flanagan, & Rollins, 2002). This test assesses an individual's ability to interpret naturalistic social interactions containing sincerity, simple sarcasm and paradoxical sarcasm. Children with ADHD demonstrated specific deficits in comprehending paradoxical sarcasm and they performed significantly less accurately than the typically developing children. While there were no significant differences between the children with ADHD and the typically developing children in their ability to comprehend sarcasm based on the speaker's intentions and beliefs, the children with ADHD were found to be significantly less accurate when basing their decision on the feelings of the speaker, but also on what the speaker had said. Results are discussed in light of difficulties in their understanding of complex cues of social interactions, and non-literal language being symptomatic of children with a clinical diagnosis of ADHD. The importance of pragmatic language skills in their ability to detect social and emotional information is highlighted

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J Neurol Neurosurg Psychiatry. 2017;88:e35.

IMPACT OF CO-MORBID ATTENTION-DEFICIT AND HYPERACTIVITY DISORDER ON COGNITIVE FUNCTION IN MALE CHILDREN WITH TOURETTE SYNDROME: A CONTROLLED STUDY.

Cavanna AE, Luoni C, Fontolan S, et al.

Objective Neuropsychological studies have highlighted the presence of specific cognitive deficits in two neurodevelopmental disorders affecting more commonly male children and often presenting in co-morbidity, Tourette syndrome (TS) and attention-deficit and hyperactivity disorder (ADHD). It is estimated that over 60% of children with TS present with co-morbid ADHD and the assessment of the relative contribution of tic symptoms and ADHD symptoms to cognitive problems in this patient population poses considerable challenges. We set out to determine the impact of co-morbid ADHD on cognitive function in male children with TS by conducting a controlled study with a comprehensive battery of neuropsychological tests.

Method Participants included four groups of unmedicated age and gender-matched children (mean age 10-12 years, range 6-15 years; 85%-100% male gender): TS group (n=13 children with a diagnosis of uncomplicated or 'pure' TS), TS+ADHD group n=8 children with TS and co-morbid ADHD), ADHD group (39 children with ADHD in the absence of tics) and controls n=66 healthy children). All patients had a DSM-validated diagnosis and were recruited from the Child Neuropsychiatry Unit, Varese, Italy, whereas healthy controls were randomly selected from a pool of research volunteers from local schools. Following clinical assessment, each participant completed a standardised battery of neuropsychological tests: the Wechsler Intelligence Scale for Children-III (Block Design test, Vocabulary test), Italian Battery for ADHD (Walk-Don't Walk test, Sustained Auditory Attention test, Stroop test, Sentence Completion test, Matching Familiar Figures test, Sustained Visual Attention test), Tower of London test, Corsi test, and Digit Span test.

Results All patient groups reported significantly lower scores than healthy controls across the neuropsychological tests involving executive functions. A specific pattern in cognitive performances emerged, showing that the TS+ADHD group was the most severely affected, followed by the ADHD group and the TS group. This was particularly evident from the results of the tests assessing planning ability (Block Design test, Matching Familiar Figures test, Tower of London test), inhibitory function (Walk-Don't Walk test, Stroop test, Matching Familiar Figures test), working memory (Sustained Auditory Attention test, Corsi test, Digit Span test) and visual attention (Walk-Don't Walk test, Matching Familiar Figures test, Sustained Visual Attention test), but not auditory attention (Sustained Auditory Attention test).

Conclusion Although problems in executive functions are more common in all patient groups than healthy controls, deficits in planning ability, inhibitory function, working memory and visual attention reported by children with TS appear to be more strongly related to the presence of co-morbid ADHD symptoms

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J Neurophysiol. 2017;118:2568-78.

ALTERED TACTILE SENSITIVITY IN CHILDREN WITH ATTENTION-DEFICIT HYPERACTIVITY DISORDER.

Puts NAJ, Harris AD, Mikkelsen M, et al.

Attention-deficit hyperactivity disorder (ADHD) is characterized by an inability to concentrate, heightened activity, and hypermotoric behavior, but sensory (e.g., tactile) problems are common. The literature on tactile impairments in ADHD is limited, with most work employing clinical observations or questionnaires. We studied tactile processing in children with ADHD and hypothesized that children with ADHD would show reduced performance in tasks closely linked to inhibition. Sixty-seven children with ADHD and 62 typically developing children (TDC) performed a battery of tasks grouped in domains: simple and choice reaction time; static and dynamic detection threshold (probing feedforward inhibition); amplitude discrimination without adaptation and with dual and single-site adaptation (probing lateral inhibition and adaptation); sequential and simultaneous frequency discrimination (previously linked to GABA); and temporal order judgment with and without a synchronous carrier stimulus. Children with ADHD could discriminate different amplitudes without adaptation, suggesting lateral inhibition is intact, but were negatively affected in all adaptation conditions, whereas TDC were only affected during single-site adaptation. Children with ADHD also showed normal frequency discrimination. Children with ADHD showed slower reaction times and higher detection threshold, likely driven by IQ and inattention, because reaction time and detection thresholds correlated with IQ and subtle motor signs. Children with ADHD showed a pattern of altered tactile processing on specific tasks, suggesting that higher cognitive function and cortical mechanisms related to adaptation are affected in

ADHD, but no clear conclusion can be drawn toward impaired inhibition. NEW & NOTEWORTHY This manuscript presents the first tactile psychophysical study testing different aspects of tactile processing in attention-deficit hyperactivity disorder (ADHD), using large cohort sizes of 67 children with ADHD and 65 Typically Developing Children. This study demonstrates impaired tactile processing in children with ADHD, on some, but not all tasks (showing this is not just due to attention), related to impaired cortical mechanisms. Furthermore, both IQ and soft motor skill abnormalities (common in ADHD) are correlated with tactile abnormalities

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J Pediatr. 2015;166:1101-04.
THE JOURNAL MEETS ANDROID.
Helton ML.

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J Pediatr. 2017.
A NATIONAL DESCRIPTION OF TREATMENT AMONG UNITED STATES CHILDREN AND ADOLESCENTS WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.
Danielson ML, Visser SN, Chronis-Tuscano A, et al.
Objective: To characterize lifetime and current rates of attention-deficit/hyperactivity disorder (ADHD) treatments among US children and adolescents with current ADHD and describe the association of these treatments with demographic and clinical factors.
Study design: Data are from the 2014 National Survey of the Diagnosis and Treatment of ADHD and Tourette Syndrome, a follow-back survey of parents from the 2011-2012 National Survey of Children's Health. Weighted analyses focused on receipt of ADHD treatment among children aged 4-17 years with current ADHD (n = 2495) by 4 treatment types: medication, school supports, psychosocial interventions, and alternative treatments.
Results: Medication and school supports were the most common treatments received, with two-thirds of children and adolescents with ADHD currently receiving each treatment. Social skills training was the most common psychosocial treatment ever received (39%), followed by parent training (31%), peer intervention (30%), and cognitive behavioral therapy (20%). Among alternative treatments, 9% were currently taking dietary supplements, and 11% had ever received neurofeedback. Most children (67%) had received at least 2 of the following: current medication treatment, current school supports, or lifetime psychosocial treatment; 7% had received none of these 3 treatment types.
Conclusions: A majority of school-aged children and adolescents with ADHD received medication treatment and school supports, whereas fewer received recommended psychosocial interventions. Efforts to increase access to psychosocial treatments may help close gaps in service use by groups currently less likely to receive treatment, which is important to ensure that the millions of school-aged US children diagnosed with ADHD receive quality treatment

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J Psychopathol Behav Assess. 2017;1-14.
WORKING MEMORY MEDIATES INCREASED NEGATIVE AFFECT AND SUICIDAL IDEATION IN CHILDHOOD ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.
Bauer BW, Gustafsson HC, Nigg J, et al.
Children with attention-deficit/hyperactivity disorder (ADHD) are at greater risk for suicidal ideation and suicide attempts compared to those without ADHD. Increased risk is at least partially attributable to a subset of children with ADHD and comorbid depression or disruptive behavior disorders; however, the early predictors and mechanisms driving increased risk are not well understood. Here, we investigate the contributions of two candidate mechanisms for increased suicidal ideation in children with ADHD: executive function and negative affect. 623 clinically well-characterized, community-recruited children classified by

research criteria as ADHD (n = 388) or typically-developing controls (n = 253) participated. Parent-report on the Temperament in Middle Childhood Questionnaire provided a measure of negative affectivity. Children completed laboratory tasks to measure response inhibition and working memory. Suicidal ideation was evaluated by parent report during a semi-structured interview and child responses on the Childrenâ€™s Depression Inventory. Compared to typically developing controls, children with ADHD had higher rates of suicidal ideation, more negative affect, slower stop signal reaction times, and weaker working memory. Statistical path-model analyses confirmed the hypothesis that weaker working memory in ADHD statistically mediated increased negative affect. Weaker working memory also mediated and increased suicidal ideation in these cross sectional data. Findings were not attributable to comorbid disruptive behavioral disorders. Poor response inhibition did not reliably mediate negative affect or suicidal ideation. Impairment in working memory is an important early risk factor for suicidal ideation in children with ADHD, and may help in identifying children for prevention and early intervention efforts

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J Trace Elem Med Biol. 2018;46:1-9.

A CROSS-SECTIONAL STUDY OF THE RELATIONSHIP BETWEEN INFANT THIMEROSAL-CONTAINING HEPATITIS B VACCINE EXPOSURE AND ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.

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

Attention-deficit/hyperactivity disorder (ADHD) is characterized by a marked pattern of inattention and/or hyperactivity-impulsivity that is inconsistent with developmental level and interferes with normal functioning in at least two settings. This study evaluated the hypothesis that infant Thimerosal-containing hepatitis B vaccine (T-HepB) exposure would increase the risk of an ADHD diagnosis. This cross-sectional study examined 4393 persons between 13 and 19 years of age from the combined 1999-2004 National Health and Nutritional Examination Survey (NHANES) by analyzing demographic, immunization, socioeconomic, and health-related variables using the SAS system. Three doses of T-HepB exposure in comparison to no exposure significantly increased the risk of an ADHD diagnosis using logistic regression (adjusted odds ratio = 1.980), linear regression (adjusted beta-coefficient = 0.04747), Spearman's rank (Rho = 0.04807), and 2 2 contingency table (rate ratio = 1.8353) statistical modeling even when considering other covariates such as gender, race, and socioeconomic status. Current health status outcomes selected on an a priori basis to not be biologically plausibly linked to T-HepB exposure showed no relationship with T-HepB. The observed study results are biologically plausible and supported by numerous previous epidemiological studies, but because the NHANES data is collected on a cross-sectional basis, it is not possible to ascribe a direct cause-effect relationship between exposure to T-HepB and an ADHD diagnosis. During the decade from 1991 to 2001 that infants were routinely exposed to T-HepB in the United States (US), an estimated 1.3-2.5 million children were diagnosed with ADHD with excess lifetime costs estimated at US $350-$660 billion as a consequence of T-HepB. Although Thimerosal use in the HepB in the US has been discontinued, Thimerosal remains in the HepB in developing countries. Routine vaccination is an important public health tool to prevent infectious diseases, but every effort should be made to eliminate Thimerosal exposure

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Metab Brain Dis. 2017;1-8.

A CROSS-SECTIONAL STUDY OF THE RELATIONSHIP BETWEEN BLOOD LEAD LEVELS AND REPORTED ATTENTION DEFICIT DISORDER: AN ASSESSMENT OF THE ECONOMIC IMPACT ON THE UNITED STATES.

Geier DA, Kern JK, Geier MR.

Attention deficit disorder (ADD) is characterized by a pattern of inattention and/or impulsivity that is inconsistent with developmental level and interferes with normal functioning in at least two settings. A recent meta-analysis suggested a significant relationship between lead (Pb) exposure and attention deficit symptoms. This study evaluated the potential relationship between increasing blood Pb levels and the risk of a reported ADD diagnosis. This cross-sectional study examined a sample of 2109 persons (32,762,158 weighted-persons) between 10 and 19 years-old from the 2003-2004 National Health and Nutritional Examination Survey (NHANES). This study analyzed demographic, socioeconomic, health related-

questions, and laboratory tests using survey logistic and frequency modeling in SAS. On a microgram (Î¼g)/deciliter (dL) basis, a significant dose-response relationship between increasing blood Pb levels and the risk of a reported ADD outcome was confirmed (odds ratio (OR) = 1.237, p = 0.0227). The relationship between increasing blood Pb levels and the risk of a reported ADD remained consistent when examining covariates such as gender, race, and socioeconomic status (OR = 1.292, p = 0.0301). Control outcomes selected on an a priori basis to not be biologically plausibly linked to blood Pb levels showed no relationship with increasing blood Pb levels. This NHANES analysis revealed an estimated 380,000 persons born in the United States (US) from 1984 to 1993 were reported to have an ADD outcome as a consequence of elevated blood Pb levels and the excess lifetime costs of these persons would be about US $100 billion. Every effort should be made to eliminate childhood Pb exposure

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Molecular Autism. 2017;8.

SPECIFICITY OF EXECUTIVE FUNCTION AND THEORY OF MIND PERFORMANCE IN RELATION TO ATTENTION-DEFICIT/HYPERACTIVITY SYMPTOMS IN AUTISM SPECTRUM DISORDERS.

Lukito S, Jones CRG, Pickles A, et al.

Background: Individuals with autism spectrum disorder (ASD) frequently demonstrate symptoms of attention-deficit/hyperactivity disorder (ADHD). Previous findings in children with ASD have suggested that these symptoms are associated with an impairment in executive function (EF) abilities. However, studies rarely considered this association within a single framework that controls for other related factors such as Theory of Mind (ToM) abilities and ASD symptoms.

Methods: We used structural equation modeling to explore the relations among EF, ToM, and symptoms of ASD and ADHD, using data from a population-based sample of 100 adolescents with ASD and full-scale IQ 50 (the Special Needs and Autism Project (SNAP) cohort). The study used a multi-measure and multi-informant approach, where performance of inhibition, planning, switching, and working memory tasks indexed EF and performance on tasks involving mentalizing indexed ToM. Measures of ASD and ADHD symptoms included parent and teacher reports and direct observation of the children. Shared source of symptom reporting was accounted for with a parental rating latent factor indexed by symptom measures reported by parents.

Results: Impairments in EF abilities were specifically associated with ADHD symptoms while impaired ToM was specifically associated with ASD symptoms, when accounting for the associations of each cognitive domain with the other factors. ASD and ADHD symptom latent factors were also correlated, but this association became nonsignificant once the shared source of reporting from parents was accounted for and within a model that also controlled for the correlated pathway between EF and ToM factors. The specific relations between the cognitive domains and behavioral symptoms remained even after controlling for IQ.

Conclusions: In this ASD sample, symptoms of ADHD and ASD are underpinned by separate cognitive domains. The association between EF and ToM impairments is a likely partial explanation for the co-occurrence of ADHD symptoms in ASD, but the role of shared reporting effects is also important and supports the inclusion of independent informants and objective measures in future research

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Nord J Psychiatry. 2017;1-6.

THE EFFECTS OF ADHD ON COGNITIVE PERFORMANCE.

Claesdotter E, Cervin M, et al.

Background: Attention-deficit hyperactivity disorder (ADHD) is a common and impairing neurodevelopmental disorder. The Cambridge Neuropsychological Test Automated Battery (CANTAB) is a computerized test battery with standardized procedures and solid psychometric properties targeting multiple neuropsychological functions.

Aims: The aim of this study was to look at the effects of ADHD on cognitive performance using CANTAB expressed as a statistical interaction term in regression modeling.

Methods: We assessed 112 drug-nave subjects (age: 7-18 years) with ADHD based on DSM IV criteria and compared them to 95 control subjects (age: 7-18 years). All participants were administered five CANTAB tasks designed to capture different aspects of executive functioning: Stockings of Cambridge (SOC), Intra/Extra dimensional shift (IED), Spatial Working Memory (SWM), Simple Reaction Time (SRT) and Stop Signal Task (SST).
Results: T-tests showed a difference between ADHD and control subjects in all cognitive measures except SOC. The majority of measures showed a non-linear effect of age. SWM strategy and SST direction errors showed a linear effect of age. ADHD diagnosis had a statistically significant effect on performance. For all tests except SOC, ADHD produced the main effect without interaction with age.
Discussion: For all CANTAB measures, ADHD diagnosis had a significant effect on performance and produced this effect without interaction with age in all tests except SOC, indicating that the developmental trajectories were parallel in both groups. The results indicate that cognitive performance is impaired in youth with ADHD and that CANTAB can be a valuable tool in the diagnostic assessment of ADHD

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Nutrients. 2017;9.

MATERNAL IODINE INTAKE AND OFFSPRING ATTENTION-DEFICIT/HYPERACTIVITY DISORDER: RESULTS FROM A LARGE PROSPECTIVE COHORT STUDY.

Abel MH, Ystrom E, Caspersen IH, et al.

Current knowledge about the relationship between mild to moderately inadequate maternal iodine intake and/or supplemental iodine on child neurodevelopment is sparse. Using information from 77,164 mother-child pairs in the Norwegian Mother and Child Cohort Study, this study explored associations between maternal iodine intake and child attention-deficit/hyperactivity disorder (ADHD) diagnosis, registered in the Norwegian Patient Registry and maternally-reported child ADHD symptoms at eight years of age. Pregnant women reported food and supplement intakes by questionnaire in gestational week 22. In total, 1725 children (2.2%) were diagnosed with ADHD. In non-users of supplemental iodine (53,360 mothers), we found no association between iodine intake from food and risk of child ADHD diagnosis ($p = 0.89$), while low iodine from food (<200 g/day) was associated with higher child ADHD symptom scores (adjusted difference in score up to 0.08 standard deviation (SD), $p < 0.001$, $n = 19,086$). In the total sample, we found no evidence of beneficial effects of maternal use of iodine-containing supplements ($n = 23,804$) on child ADHD diagnosis or symptom score. Initiation of iodine supplement use in gestational weeks 0 12 was associated with an increased risk of child ADHD (both measures). In conclusion, insufficient maternal iodine intake was associated with increased child ADHD symptom scores at eight years of age, but not with ADHD diagnosis. No reduction of risk was associated with maternal iodine supplement use

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Pediatr Diabetes. 2017;18:52-53.

PREVALENCE OF ATTENTION-DEFICIT/HYPERACTIVITY DISORDER IN CHILDREN AND ADOLESCENTS WITH EARLY ONSET TYPE 1 DIABETES COMPARED TO GENERAL POPULATION PEERS.

Castillo K, Stahl-Pehe A, BÃ¤chle C, et al.

Objective: To analyze the prevalence of diagnosed attention-deficit/ hyperactivity disorder (ADHD) in 11- to 17-year-olds with type 1 diabetes (T1D) and peers from the general population in Germany and characterize differences between groups.
Methods: Data from T1D patients participating in population-based, nationwide questionnaire surveys (conducted 2009-2010 and 2012- 2013) were compared with data from the representative German KiGGS Follow-Up telephone-based survey (KiGGS wave 1, 2009- 2012). Patients were classified as having ADHD if they had previously been diagnosed by a doctor or psychologist. Multiple logbinomial regression analyses were conducted adjusting for socioeconomic and demographic covariates.
Results: T1D patients (N=1037) comprised 51.3% boys, 27.3% were children (11-13 years) and the mean diabetes duration was 12.2 (SD 1.4) years. Among KiGGS participants (N=5188) 51% were boys and 43.2% were children. The overall prevalence of ADHD diagnosis was estimated to be 6.6% in the T1D group and

6.1% in peers (adjusted relative risk (RR)=1.14 [95%-CI 0.88-1.47; p=0.313]). But the risk for ADHD in T1D patients compared to peers was only higher in girls (adjusted RRgirls=1.90 [95%-CI 1.17-3.07; p=0.009]) and not in boys (adjusted RRboys=0.97 [95%-CI 0.72-1.31; p=0.849]). Among ADHD cases, the frequency of boys was similar in both samples (68.6% in T1D study vs. 80.6% in (KiGGS), adjusted RR=0.84 [95%-CI 0.71-1.01; p=0.065]). In addition, the proportion of adolescents in the age group 14-17 years was higher in the T1D study than in the KiGGS group (72.5% vs. 56.7%), adjusted RR=1.25 [95%-CI 1.04-1.50; p=0.015]). No differences were found between T1D patients and peers with ADHD regarding the possible associations with socio-economic status and family structure.
Conclusion: Prevalence of diagnosed ADHD was similar between children and adolescents with T1D and their peers. However, differences were observed regarding age and sex distributions

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Pediatr Drugs. 2017;1-14.
DEVELOPMENT OF GUANFACINE EXTENDED-RELEASE DOSING STRATEGIES IN CHILDREN AND ADOLESCENTS WITH ADHD USING A PHYSIOLOGICALLY BASED PHARMACOKINETIC MODEL TO PREDICT DRUG DRUG INTERACTIONS WITH MODERATE CYP3A4 INHIBITORS OR INDUCERS.
Li A, Yeo K, Welty D, et al.
Background: Guanfacine extended-release (GXR) is an orally administered, non-stimulant treatment for children and adolescents with attention-deficit/hyperactivity disorder (ADHD) and is primarily metabolized by the 3A4 isozyme of cytochrome P450 (CYP3A4). The results of clinical pharmacokinetic (PK) studies indicate that guanfacine is sensitive to drug drug interactions (DDIs) perpetrated by strong inhibitors and inducers of CYP3A4.
Objective: The aim was to provide guidance on the possible requirement for GXR dose adjustment in children and adolescents with ADHD by predicting DDIs following co-administration with moderate CYP3A4 inhibitors and inducers.
Methods: A physiologically based PK model for GXR orally administered to healthy adults was developed based on physicochemical, in vitro and clinical PK data. The model was validated using clinical PK data for co-administration of GXR with ketoconazole (strong CYP3A4 inhibitor) or rifampicin (strong CYP3A4 inducer).
Results: Model predictions indicated that co-administration of GXR with the moderate CYP3A4 inhibitors erythromycin 500 mg three times a day or fluconazole 200 mg daily (q.d.) increased the guanfacine area under the plasma concentration-time curve (AUC) by 2.31-fold or 1.98-fold, respectively, compared with GXR monotherapy. The moderate CYP3A4 inducer efavirenz 400 mg or 600 mg q.d. was predicted to reduce guanfacine AUC to 58 or 33% of its value for GXR monotherapy, respectively.
Conclusion: Without the requirement for additional clinical studies, the following GXR dose recommendations were developed and approved for US labeling for use in children and adolescents with ADHD: (1) decrease GXR to 50% of the usual target dose when it is co-administered with strong or moderate CYP3A4 inhibitors; (2) consider titrating GXR up to double the usual target dose over 1-2 weeks when it is co-administered with strong or moderate CYP3A4 inducers

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Prog Neuro-Psychopharmacol Biol Psychiatry. 2018;81:169-77.
ASSOCIATION OF PIK3CG GENE POLYMORPHISMS WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER: A CASE-CONTROL STUDY.
Gu X, Yuan F-F, Huang X, et al.
Attention-deficit/hyperactivity disorder (ADHD) is a complicated neurodevelopmental disorder with high heritability. This study explores the association of PIK3CG gene single nucleotide polymorphisms (rs1129293, rs12536620, rs12667819, rs17847825, rs2230460) with ADHD in children and the relation of interaction between SNPs and environmental factors, including blood lead levels (BLLs) and feeding style. A case-control study was conducted with children aged 6 18 years old, consisting of 389 children newly diagnosed with ADHD via the DSM-IV at the Wuhan Women and Children Medical Care Center, and 393

control participants were healthy children for physical examination during the same period. All participants were tested using the Chinese Wechsler Intelligence Scale for Children and Parent Symptom Questionnaire (PSQ). Furthermore, a self-designed questionnaire was used to investigate the general situation and related environmental factors, and the BLLs were measured by atomic absorption spectrophotometry. The genotyping was performed using Sequenom MassArray. In our study, PIK3CG gene rs12667819 was consistently shown to be associated with ADHD risk in dominant model (OR = 1.656, 95% CI = 1.229 2.232), ADHD-I type (OR = 2.278, 95% CI = 1.666 4.632), and symptom scores. Moreover, rs12536620 has been observed to be related to ADHD-C type and symptom scores. Intriguingly, gene-environmental interactions analysis consistently revealed the potential interactions of rs12667819 collaborating with blood lead (Pmul = 0.045) and feeding style (Pmul = 0.041) to modify ADHD risk. Expression quantitative trait loci analysis suggested that rs12667819 may mediate PIK3CG gene expression. Therefore, our results suggest that selected PIK3CG gene variants may have a significant effect on ADHD risk

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Psychiatr Invest. 2017;14:808-16.

THE ROLE OF UNCONTROLLED EATING AND SCREEN TIME IN THE LINK OF ATTENTION DEFICIT HYPERACTIVITY DISORDER WITH WEIGHT IN LATE CHILDHOOD.

Ahn J-S, Min S, Kim M-H.

Objective The aim of this study was to examine the mediating roles of uncontrolled eating and sedentary behaviours in the link of attention deficit hyperactivity disorder (ADHD) and weight.

Methods A total of 352 children in fifth and sixth grade participated in the present study by completing the self-rated Three-Factor Eating Questionnaire and Children of Alcoholics Screening Test during regular classes. An additional questionnaire completed by their parents provided information about the children's ADHD and emotional symptoms, sedentary behaviour based on screen time, and parental variables. The questionnaires were surveyed within one week after their schools annual physical check-up.

Results Hierarchical regression analyses revealed that uncontrolled eating was complete mediator in association between ADHD symptoms and body mass index (BMI) for boys, incomplete mediator for girls. However, screen time had no significant effect on the ADHD symptoms-BMI link for both gender.

Conclusion The findings of this study suggest that gender specific intervention programs may be need to help eating behaviour in children with ADHD and overweight

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Psychiatry Res Neuroimaging. 2017.

REDUCED SUBCORTICAL VOLUMES AMONG PRESCHOOL-AGE GIRLS AND BOYS WITH ADHD.

Rosch KS, Crocetti D, Hirabayashi K, et al.

Anomalous brain structure and function are implicated in children with attention-deficit/hyperactivity disorder (ADHD). Most neuroimaging research, however, has examined school-aged children, despite the typical onset of symptoms in early childhood. This study compared the volumes of subcortical structures (caudate nucleus, putamen, globus pallidus, and thalamus) among preschoolers with ADHD and typically developing (TD) children. High resolution T1-weighted 3D MPRAGE images covering the whole brain were acquired on a 3T scanner and subcortical volumes were automatically extracted. Analyses were conducted in a total of 87 medication-naÃ¯ve preschoolers, ages 4-5 years (47 with ADHD, 40 controls; 63% boys). ADHD was diagnosed using modified DSM-IV criteria based on review of developmental history, structured psychiatric interview and caregiver ratings. Compared to typically developing children, subcortical volumes were reduced among preschoolers with ADHD, with largest reductions in the caudate, globus pallidus, and thalamus. Among girls (but not boys) with ADHD, putamen and thalamus volumes were associated with ADHD symptom severity. The observed patterns of subcortical differences in preschoolers with ADHD (larger reductions in girls), contrasted with differences observed among school-aged children, (larger reductions in

boys) suggests that children with ADHD show sexual dimorphism in neuroanatomical development that parallels early trajectory of symptom onset and attenuation

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Psychiatry Res. 2017;258:611.

THE MULTIPLE PHENOTYPES OF TOURETTE SYNDROME AND ATTENTION-DEFICIT HYPERACTIVITY DISORDER.

Termine C, Luoni C, Fontolan S, et al.

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Psychoneuroendocrinology. 2016;71:33.

MATERNAL DEPRESSION DURING PREGNANCY IS ASSOCIATED WITH CHILD ADHD SYMPTOMS AT 3.5 YEARS.

Wolford E, Pesonen A-K, Lahti M, et al.

Background: Maternal depressive symptoms during pregnancy have been associated with child attention deficit/hyperactivity disorder (ADHD) symptoms in early childhood. However, it is still unknown if feeling depressed throughout pregnancy is more harmful to the child than feeling depressed at some point in time, or if maternal ADHD problems or maternal depressive symptoms at the assessment of child symptoms account for or add to the prenatal effects.

Methods: Our study sample (2312 mother-child dyads, 50.6% boys) comes from the multidisciplinary Prediction and Prevention of Pre-eclampsia and Intrauterine Growth Restriction (PREDO) study. Mothers reported their depressive symptoms biweekly up to 14 times during pregnancy. When the children were 3.5 years old (range 1.9-6.3 years), the mothers filled out questionnaires on their own ADHD problems, depressive symptoms, and their children's ADHD symptoms.

Results: Higher maternal depressive symptoms throughout pregnancy were associated with higher ADHD symptoms in the child ($p < 001$). The effects stayed significant even after adding maternal ADHD problems or depressive symptoms to the linear regression model (p-values < 001). Child ADHD symptoms increased according to the number of times maternal depressive symptoms were reported to be at a clinically significant level at the first, second, and third pregnancy trimesters (p-values for linear trend < 001).

Conclusions: Depressive symptoms across pregnancy predict increased mother-reported ADHD symptoms in young children in a gestation-week non-specific way. Yet, feeling depressed throughout pregnancy seems to be more harmful to the child than feeling depressed for only part of the time. This effect is not explained by maternal ADHD problems or maternal mood at the time child behavior is assessed

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Psychoneuroendocrinology. 2017;83:30-31.

INFLUENCE OF BODY-ORIENTED THERAPY ON EXECUTIVE ABILITIES IN ADHD CHILDREN.

Kiselev S, Parshakova A.

Objectives: It is known that children with ADHD have deficits in executive abilities. The gaol of this study was to reveal the effect of body-oriented therapy on executive abilities in ADHD children. Particularly 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: 16 children with ADHD between 7 and 8 years of age were included and randomly assigned to treatment conditions according to a 2Ã—2 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 (0.57-0.91).

Conclusions: The findings from this pilot study suggest that body-oriented therapy can effectively influence the executive abilities in children with attention-deficit hyperactivity disorder. However, it is necessary to

further research the impact of bodyoriented therapies on the prevention and treatment of ADHD in children. The research was supported by Russian Foundation for Basic Research, grant no. 15-06-06491A

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Res Dev Disabil. 2018;72:96-105.

SUICIDE RISK REDUCTION IN YOUTHS WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER PRESCRIBED METHYLPHENIDATE: A TAIWAN NATIONWIDE POPULATION-BASED COHORT STUDY.

Liang SHY, Yang Y-H, Kuo T-Y, et al.

Background Attention-deficit/hyperactivity disorder (ADHD) youths have increased suicide risk. Nevertheless, the beneficial effects of methylphenidate (MPH) on suicide attempt have received relatively little attention.

Aims To investigate the MPH usage and the risk of suicide attempt among ADHD youths.

Methods We identified 84,898 youths less than 18 years old with ADHD diagnosis between 1997 and 2013 from National Health Insurance, and examined whether MPH use affected suicide attempt risk using Cox proportional-hazards models.

Outcome and results Among ADHD youths, reduction of suicide risk was found in patients prescribed 90-180 days of MPH after adjusting for confounding factors (hazard ratio (HR): 0.41, 95% confidence interval (CI): 0.19-0.90) and a greater reduction in those prescribed more than 180 days of MPH (HR: 0.28, 95% CI: 0.17-0.48).

Conclusions and implications We observed a 59% suicide attempt risk reduction among ADHD youths prescribed between 90 and 180 days and a 72% risk reduction in those prescribed more than 180 days of MPH. The protective benefit observed by the group prescribed MPH for longer duration underscores the importance of psychoeducation and compliance enhancement as part of ADHD management. Indication bias is identified as a limitation of this study, and future self-case control study to investigate the association between suicide attempt and ADHD medication is suggested. What this paper adds This nationwide population-based cohort study showed that among ADHD youths, reduction of suicide risk was observed in patients prescribed MPH for duration 90 days and longer, underscoring the importance of appropriate ADHD pharmacotherapy and enhancing drug compliance

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Rev Neurol. 2017;64:413-21.

EVALUATION AND TREATMENT OF SLEEP PROBLEMS IN CHILDREN DIAGNOSED WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER: AN UPDATE OF THE EVIDENCE.

Chamorro M, Lara JP, Insa I, et al.

Introduction. Attention deficit hyperactivity disorder (ADHD) affects approximately 5% of all children and adolescents, and these patients frequently suffer from sleep problems. The association between sleep disorders and ADHD, however, is multifaceted and complex.

Aims. To explore the relationship between sleep disorders and ADHD.

Development. Sleep problems in children with ADHD include altered sleep and specific disorders per se or that may be due to comorbid psychiatric disorders or to the stimulants they receive as treatment for their ADHD. Today, an evaluation of the sleep conditions in children with ADHD is recommended before starting pharmacological treatment. The first step in managing their sleep problems is good sleep hygiene and cognitive-behavioural psychotherapy. Another option is to consider modifying the dosage and formulation of the stimulants. Atomoxetine and melatonin are therapeutic alternatives for children with ADHD and more severe sleep problems. Specific treatments exist for respiratory and movement disorders during sleep.

Conclusions. It is important to evaluate sleep in children who present symptoms suggestive of ADHD, since problems during sleep can play a causal role or exacerbate the clinical features of ADHD. Correct evaluation and treatment of sleep disorders increase the family's and the childs' quality of life and can lessen the severity of the symptoms of ADHD

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Rev Neurol. 2017;65:145-52.

EMOTIONAL FACIAL RECOGNITION DIFFICULTIES AS PRIMARY DEFICIT IN CHILDREN WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER: A SYSTEMATIC REVIEW.

Rodrigo-Ruiz D, et al.

Introduction. It has recently been warned that children with attention deficit hyperactivity disorder (ADHD) show a deficit in emotional competence and emotional intelligence, specifically in their ability to emotional recognition.

Patients and methods. A systematic review of the scientific literature in reference to the emotional recognition of facial expressions in children with ADHD is presented in order to establish or rule the existence of emotional deficits as primary dysfunction in this disorder and, where appropriate, the effect size of the differences against normal development or neurotypical children.

Results. The results reveal the recent interest in the issue and the lack of information. Although there is no complete agreement, most of the studies show that emotional recognition of facial expressions is affected in children with ADHD, showing them significantly less accurate than children from control groups in recognizing emotions communicated through facial expressions. A part of these studies make comparisons on the recognition of different discrete emotions; having observed that children with ADHD tend to a greater difficulty recognizing negative emotions, especially anger, fear, and disgust.

Conclusions. These results have direct implications for the educational and clinical diagnosis of ADHD; and for the educational intervention for children with ADHD, emotional education might entail an advantageous aid

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Rev Neurol. 2017;64:299-304.

RESTLESS LEGS SYNDROME IN PATIENTS DIAGNOSED WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER.

De La Mota C, Moreno-Acero N, Losada-Del PR, et al.

Introduction. Restless legs syndrome (RLS) is a common neurological disease. RLS has been linked to various psychiatric disorders, especially with attention deficit hyperactivity disorder (ADHD).

Aims. The main objective was to describe the frequency of RLS in pediatric patients diagnosed with ADHD. Secondary objectives of the study were describe other sleep disorders in ADHD patients.

Patients and methods. A multicentre prospective study was conducted in nine Spanish centers. We included children aged 6-18 years diagnosed with ADHD between January and June 2015. Data were collected by 13 researchers doctors through an interview with the parent/caregiver and with the child. To assess the degree of functioning of patients with ADHD we used the Children's Global Assessment Scale. The Sleep Disturbance Scale for Children was applied to screening sleep disorders in childhood.

Results. A sample of 73 patients was collected. Five patients (6.8%) met diagnostic criteria for RLS: four of them definitive and one probable.

Conclusions. RLS is a frequent condition in adulthood but also in adolescence and childhood. ADHD patients have an increased risk of an RLS

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Schizophr Bull. 2017;43:1036-44.

BULLYING MEDIATES BETWEEN ATTENTION-DEFICIT/HYPERACTIVITY DISORDER IN CHILDHOOD AND PSYCHOTIC EXPERIENCES IN EARLY ADOLESCENCE.

Hennig T, Jaya ES, Lincoln TM.

Although a childhood diagnosis of attention-deficit/ hyperactivity disorder (ADHD) is known to be linked to psychotic experiences and psychotic disorders in later life, the developmental trajectories that could explain this association are unknown. Using a sample from the prospective population-based Avon Longitudinal Study of Parents and Children (ALSPAC) (N = 8247), we hypothesized that the previously reported association of ADHD combined subtype in childhood and psychotic experiences in early adolescence is mediated by traumatic events and by involvement in bullying. Moreover, we expected this mediation to be

specific to ADHD and tested this by comparison with specific phobia. Children with ADHD combined subtype at age 7 were more often involved in bullying at age 10 (OR 3.635, 95% CI 1.973-6.697) and had more psychotic experiences at age 12 (OR 3.362, 95% CI 1.781-6.348). Moreover, children who were involved in bullying had more psychotic experiences (2.005, 95% CI 1.684-2.388). Bullying was a significant mediator between ADHD and psychotic experiences accounting for 41%-50% of the effect. Traumatic events from birth to age 11 were also significantly associated with ADHD combined subtype and psychotic experiences; however, there was no evidence of mediation. Specific phobia was significantly associated with psychotic experiences, but not with bullying. To conclude, bullying is a relevant translating mechanism from ADHD in childhood to psychotic experiences in early adolescence. Interventions that eliminate bullying in children with ADHD could potentially reduce the risk of having psychotic experiences in later life by up to 50%. Clinicians should thus screen for bullying in routine assessments of children with ADHD

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Technol Health Care. 2017;25:877-85.

EVALUATING THE FEATURES OF THE BRAIN WAVES TO QUANTIFY ADHD IMPROVEMENT BY NEUROFEEDBACK.

Dehghanpour P, Einalou Z.

BACKGROUND: Attention-deficit/hyperactivity disorder (ADHD), as one of the most common neurological disorders in children and adolescents, is characterized by decentralization, slow learning, distraction and hyperactivity. Studies have shown that in addition to medication, neurofeedback training can also be used to partially control the brain activity of these patients.

METHODS: In this study, using the brain signals processing before and after the treatment in 10 children treated by neurofeedback, the changes were evaluated by non-parametric statistical analysis and impact of neurofeedback on brain frequency bands was investigated. Finally, the results were compared with the protocols introduced in this paper and before researches.

RESULTS: The results of Kruskal-Wallis test showed an approximately significant increase in the relative power of gamma and an approximately significant reduction in the ratio of relative power of alpha/beta.

CONCLUSIONS: It represents the emotional response, elicited by the successful learning and diminished ratio of slow learning to active learning respectively

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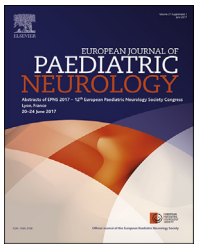

Abstracts of EPNS 2017 – 12th European Paediatric Neurology Society Congress, 20–24 June 2017, Lyon, France

ORAL COMMUNICATIONS

Wednesday, June 21

Parallel Sessions 10:30 – 12:15

EPILEPSY 1

PS 2: Invited Lecture
Psychiatric comorbidities in children with epilepsy: Do they differ from adults?

Lieven Lagae. *Belgium*

http://dx.doi.org/10.1016/j.ejpn.2017.04.679

OC7
Neuropsychiatric disorders and psychopathology of children and adolescents with Tuberous Sclerosis

Irene Toldo, Valeria Brasson, Marina Miscioscia, Samuela Bugin, Renzo Manara, Margherita Nosadini, Marilena Vecchi, Stefano Sartori, Michela Gatta. *Department of Woman's and Child's Health, University Hospital of Padua, Italy*

Objective: To evaluate Tuberous Sclerosis (TS) associated neuropsychiatric disorders (TAND) and the caregiving's experience and the parenting stress in patients with TS. **Methods**: A prospective study was conducted on a cohort of children and adolescents affected by TS. The following tests/questionnaires were administered: TAND-checklist (de Vries P.J. et al., 2015), CBCL, VABS, ECI, FES and PSI, Raven matrices (5–18 years). Moreover to adolescent patients (≥11 years; IQ> 70): YSR, MASC, CDI, SF-36 and TAS. Clinical and neuroradiological features were analyzed for each patient. Two neurological outcome scores (EGOS-ped and E-Chess score modified) were applied at last follow-up. **Results**: 32 patients aged 1 to 19 years (mean 9.8 y) participated to the study. 87% of subjects had at least one TAND and 47% of cases had intellectual disability. TAND-Checklist interview revealed internalizing problems in 65% of cases (vs 42% of cases found by CBCL) and externalizing problems in 84% of cases (vs 10% of cases found by CBCL). VABS results correlated with age at TS diagnosis, number of brain tubers and ratings to EGOS-PED and E-Chess score. 39% of mothers and 31% of fathers reported difficult parent-child interaction. **Conclusions**: We found the TAND-Checklist was effective in the detection of psychopathology and more precise, in some aspects, than CBCL. In our sample the following TANDs prevailed: attention deficit, speech impairment, intellectual disability, difficulties at school and poor relationships with peers. Each patient had an unique neuropsychiatric profile. Genetics, family history for TS, neuroradiological features, neurological outcomes, the presence of mental retardation and the age of onset of epilepsy correlated with some TANDs. TAND-checklist and the other questionnaires could be extensively used in clinical practice and would allow an early detection of neuropsychiatric disorders and caregiving difficulties thus contributing to improve quality of life of patients and their families.

http://dx.doi.org/10.1016/j.ejpn.2017.04.680

OC8
Prospective neuropsychiatric follow up in TSC infants from diagnosis to 12 months

L. Ouss[a,b], D. Breuillard[a,b], N. Chemaly[a,b], N. Bahi Buisson[a,b], M. Hully[a,b], I. Desguerre[a,b], R. Nabbout[a,b]. [a]*Reference Centre for Rare Epilepsies and Tuberos Sclerosis Complex, Department of Pediatric Neurology, Necker Enfants Malades Hospital, Paris, France.* [b]*Child Psychiatry Unit, Necker Enfants Malades Hospital, Paris, France*

Objectives: A large proportion of children with TSC develop TSC Associated Neuropsychiatric Disorders (TAND), including Autism Spectrum Disorders. The increasing number of patients with antenatal or precocious diagnosis opened a window for early detection of TAND in infants, as we know that early interventions modify the outcome of infants at risk for developmental disorders. We aimed to study early psycho-motor and psycho-affective/interactive development in children with TSC in their first year of life, using standardized tools. **Methods**: We assessed the development of children with a prenatal or a first year of life diagnosis of TSC, with a genetic and neurological assessment, according to three dimensions: (1) psychomotor development (Brunet Lezine), with a focus on language (Mac Arthur Inventory) and motor development (DF MOT) (2) psycho-affective development : temperament (ICQ), and interactive behaviour during recorded standardized interactive sessions with the mother (CIB), (3) ASD screening (PREAUT grid, CSBS DP). Evaluations were made at 3 key time points of development: 6, 9 and 12 months. **Results**: Fourteen patients aged <12 months were included. TSC diagnosis was made AN in 5 and between age D2 and M6 in 9. Developmental scores show a deterioration of the developmental quotients from 6 to 12 months and a specific impairment in oculo-manual coordination. Psycho-affective development and ASD screening results are detailed with an interest in the seizures onset and type, and neuropsychiatric development. **Conclusion**:

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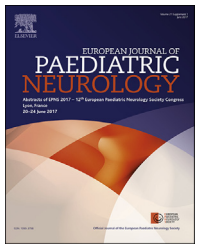

Abstracts of EPNS 2017 – 12th European Paediatric Neurology Society Congress, 20–24 June 2017, Lyon, France

POSTER PRESENTATIONS

Thursday, June 22

NEUROPSYCHIATRY

P2-139
Social cognition in children with 22q11 deletion syndrome

Elodie Peyroux, Marie Noëlle Babinet, Caroline Demily, Costanza Cannarsa, George Michael. *GENOPSY – Centre régional de dépistage et de prises en charge des troubles psychiatriques d'origine génétique – CH Le Vinatier, France*

Objective: 22q11 deletion syndrome is the most common microdeletion syndrome in the general population. Neurocognitive and social cognitive impairments are frequently observed in people with 22q11 deletion syndrome. Nevertheless, only few studies have examined the links between social cognition and both neurocognitive impairments and social functioning. However, social cognition seems to play the role of mediator between neurocognition and behavior in other psychiatric populations such as schizophrenia. **Methods:** In this study, we compared two groups of participants from 5 to 13 years old: a group of 20 children carrying microdeletion 22q11 and a group of 20 healthy controls matched in age and sex. We used a new experimental paradigm (ACQUISS) assessing 3 components of social cognition: facial emotion recognition, social situations understanding and vocal emotion recognition. In addition, we studied links between social cognitive measures and both attentional and visuo-spatial abilities, and we assessed impacts of social cognitive impairments on both components of functioning, such as aggression or behavioral disorders, and clinical features, such as depression and attentional disorders. **Results:** Patients with 22q11 deletion syndrome had significantly lower results in the three components of social cognition assessed (facial emotions recognition: controls=88%; 22q11=76%; p<.01; social situations understanding: controls=72%; 22q11=49%; p<.01; and vocal emotion recognition: controls=81%; 22q11=46%; p<.01). However, results did not show any significant impact of attentional and/or visuospatial processes on social cognitive abilities. Moreover results obtained by participants in ACQUISS'tasks did not predict the behavioral disorders of patients with 22q11 deletion syndrome. **Conclusion:** These results contribute to the understanding of social cognitive impairment in population of children with 22s11 deletion syndrome. Researches concerning the relationships between social cognition and both cognitive deficits and functioning in daily life had to be continued.

http://dx.doi.org/10.1016/j.ejpn.2017.04.1284

P2-140
Correlation between sleep disorders and ADHD in children with absence epilepsy: An observational study

Maddalena Duca[a,b], Carlo Cottone[a,b], Lucia Maltoni[a,b], Matteo Migliori[a,b], Antonia Parmeggiani[a,b], Emilio Franzoni[a], Leslie Nollace[a,b], Vania Herbillon[a,b], Faustine Ilski-Lecoanet[a,b], Julitta De Bellescize[a,b], Eleni Panagiotakaki[a,b], Patricia Franco[a,b], Alexis Arzimanoglou[b]. *[a]UO Neuropsichiatria Infantile, Azienda Ospedaliero Universitaria Policlinico S. Orsola-Malpighi, Bologna, Italy. [b]Department of Pediatric Clinical Epileptology, Sleep Disorders and Functional Neurology, University Hospitals of Lyon, Lyon, France*

Objective: The authors investigated sleep disorders (SD) and ADHD in children with absence epilepsy (AE) and the correlation with adverse effects of antiepileptics drugs (AED). **Methods:** Inclusion criteria: age 5-16 years, epilepsy with typical absences diagnosis, normal neurological examination. Parents completed questionnaires on sleep, AED side effects, school performances, learning problems, ADHD rating scale. Results were compared to an healthy sample. Our population was then divided into 2 groups: with and without seizures at last examination. Number, gender, family and personal history for epilepsy or febrile convulsions, AED, neuropsychological tests results when available, presence of SD were analyzed. The statistical relationships between a) SD and ADHD with AED adverse effects, b) SD and ADHD symptoms, c) the variance analysis between ADHD and SD considering the presence of seizures with the adverse effects as covariate, were considered. **Results:** Seventy children with absence seizures were included in the study; 59% controlled by AED. Neuropsychological evaluation was performed in 63%, in 51% identifying one or more deficient domains. 50% had ADHD clinical diagnosis, ADHD Rating scale, performed by all sample, was positive in 37%. SD were reported in 43 % of patients: 21% breath disorders, 16% insomnia, 19% parasomnia, 11% non-restoring sleep and 11% excessive sleepiness. Statistical difference for SD was found between children with epilepsy and healthy controls ($p < 0.001$), no difference in SD between subgroups with and without seizures; statistical correlation respectively of SD ($p<0.001$), and ADHD ($p=0.000$) with

AD adverse effects, significative correlation between SD and ADHD (p=0.000). **Conclusion:** SD are not rare in children with AE. ADHD symptoms may also be present. In everyday clinical practice we advise a systematic investigation of this children, using validated questionnaires, ideally at epilepsy diagnosis and before treatment. A control at 6 months would allow early detection of eventual comorbidities and appropriate adjustment of therapeutic strategies.

http://dx.doi.org/10.1016/j.ejpn.2017.04.1285

P2-141
Narcolepsy in children: A severity of the disease does not differ from adults

S. Nevsimalova, J. Pisko, K. Sonka. *Department of Neurology, Charles University, Prague, Czech Republic*

Objective: Narcolepsy is a life-long disease with abnormal regulation of the sleep-wake cycle and increased penetration of rapid eye movement (REM) sleep. Narcolepsy type 1 (NT1) is characterized by excessive daytime sleepiness, cataplexy, disturbed nocturnal sleep, and occasionally accompanied by hypnagogic hallucinations and sleep paralysis. Narcolepsy type 2 (NT2) has a similar clinical course, however, without cataplexy. **Methods:** 38 pediatric patients (28 NT1, 10 NT2) in whom the disease had developed before the age of 18 years (mean age 13.2±3.6 years) were collected and correlated with a group of adult patients (n=117). All patients underwent clinical examination, polysomnographic (PSG) monitoring followed by multiple sleep latency test (MSLT) and Epworth Sleepiness Scale (ESS) measurement. **Results:** A proportion of NT1 cases (73.7% children vs. 79.5% adults) were similar in both groups. Also the occurrence of hypnagogic hallucinations (50% vs. 54.7%) and sleep paralysis (39.5% vs. 37.6%) was almost equal. Frequent symptoms in children were sleep inertia during awakening, unquiet nocturnal sleep accompanied by nightmares, behavioral and serious school problems. An exceptionally severe case of daytime sleepiness with automatic behavior and cataplexy was found in a 13-year-old boy in whom a heterozygote deletion (size 3.4 Mb) of 1 p chromosome was verified. BMI was higher (p<0.05) in NT1 patients (similarly as in adults). Sleepiness confirmed a high ESS score (17.4±2.5 in children, 18.0±3.4 in adults). Mean MSLT latency was 3.4 ±2.8 min with 3.4±1.3 sleep onset REM periods (SOREMs) in children, with the results showing no difference from those in the adults (2.7±2.1 min, 3.3±1.1 SOREMs). **Conclusion:** The clinical course and severity of the disease in narcoleptic children are comparable to those in adults. Only so called "cataplectic facies" is the main distinction in early childhood as a feature likely to disappear before puberty.

http://dx.doi.org/10.1016/j.ejpn.2017.04.1286

P2-142
The clinical characteristics of attention deficit hyperactivity

M. Mahajnah, N. Zelnik. *Child development and pediatric neurology center, Hillel Yaffe Medical center, The Ruth and Bruce Rappaport Faculty of Medicine, Technion, Haifa, Israel*

Objective: Identifying the clinical characteristics in adolescents newly diagnosed with ADHD. **Methods:** Data of patients aged 7-17 years diagnosed with ADHD was collected and analyzed. The patients divided into adolescents aged 13-17 years (Group I) and children aged 7-12 years (Group II), 592 males and 231 females. Group Iconsists of 450 subjects, Group II 373 subjects. **Results:** Adolescents were predominantly inattentive (63.8%), most of Group II patients had combined or hyperactive ADHD (70.8%). Learning Disorders more common in adolescents (51.2% vs. 39.7%) and treated mainly with long- acting methylphenidate, Group II patients were treated mainly with short and medium-acting methylphenidate. Newly diagnosed adolescents were less likely to exhibit behavioral comorbidities. Headache and insomnia were reported more in adolescents, stimulant rebound effect was more in younger children. **Conclusion:** While the biological nature of ADHD is similar in both age groups the primary symptomatology and associated comorbidities are prone to age- dependent changes.

http://dx.doi.org/10.1016/j.ejpn.2017.04.1287

P2-143
Level of parental anxiety and use of antipyretics in childhood fever

Lupusor Nadejda, Revenco Nineli, Holban Ala, Lupusor Adrian, Hadjiu Svetlana. *Department of Pediatrics, Clinic of Child's neurology, State University of Medicine and Pharmacy "Nicolae Testemitanu" Chisinau, Republic of Moldova*

Objective: The aim of the study was to analyse parental fever management (degree of temperature when parents start to administrate antipyretics) in relationship with the level of parental anxiety. **Methods:** Parental fever management was assessed by a questionnaire; the anxiety was determined by Spielberger-Hanin State-Trait Anxiety Inventory. There were surveyed 246 parents (median age 28,5 ± 5,7 years) of children, aged 3 months to 5 years, admitted to hospital with fever, without coexisting serious illness. **Results:** We have found that parents with a high level of anxiety (both – state and trait), administrate antipyretics at low degree of child's temperature – 37.0 – 37.5 C in comparison with the parents with normal level of anxiety which administrate antipyretics at 38.5-39.0 C (trait anxiety- p<0,005, state anxiety- p<0,005). The most frequent fears about fever were that it can generate serious health complications, loss of consciousness, stroke, coma, choke. **Conclusion:** Childhood fever management – antipyretic administration – depends on the level of parental anxiety which is generated by misconceptions about the harmful effects of fever. Early antipyretic administration can reduce the beneficial effects of fever for child recovery.

http://dx.doi.org/10.1016/j.ejpn.2017.04.1288

P2-144
Attention deficit hyperactivity disorder in pediatric patients with malignant hematologic diseases and epilepsy: Experience at a Tertiary Care Hospital in Korea

Ji Yoon Han, In Goo Lee, Hyo Sup Kim. *Daejeon St. Mary's Hospital, South Korea*

Objective: Pediatric patients with epilepsy and malignant hematologic diseases (MHD) are at increased risk of mental health problems compared to the general population. The purpose of this study is to identify the prevalence of attention-deficit hyperactivity disorders (ADHD) among pediatric patients treated for MHD and epilepsy in Korea. **Methods:** We retrospectively reviewed 184 patients diagnosed with epilepsy and 172 patients diagnosed with malignant hematologic diseases in pediatric departments of Seoul St. Mary's hospital from May 2009 to May

Thailand; [2]Chiang Mai University, Department of Psychiatry, Faculty of Medicine, Chiang Mai, Thailand; [3]Ramathibodi Hospital, Mahidol University, Department of Psychiatry, Faculty of Medicine, Bangkok, Thailand; [4]Chiang Mai University, Psychiatric Nursing Division, Faculty of Nursing, Chiang Mai, Thailand

Background: Some clinical trials suggested that risperidone was beneficial in the treatment of autism spectrum disorders (ASD) in children and adolescents. Since such studies had small sample sizes, a systematic review, a more powerful method for estimating the true effect size, may be appropriate strategy to validate the efficacy, acceptability and tolerability of risperidone in the treatment of those patients.

Objectives: Aim of this systematic review was to determine the efficacy, acceptability and tolerability of risperidone in treatment of children and adolescents with ASD.

Data Sources: The databases of Scopus, PubMed, CINAHL and Cochrane Controlled Trials Register were searched in March 2017. All randomized controlled trials (RCTs) of ASD in children and adolescents were eligible for present review.

Study Eligibility Criteria, Participants, and Interventions: Eligible RCTs of risperidone in the acute treatment of child and adolescent patients with ASD had to report end point outcomes relevant to: (i) severity of ASD, (ii) response rate, (iii) overall discontinuation rate, or (iv) discontinuation rate due to adverse events. In case of more one fixed-dose risperidone regimen, only the highest dose group was included. Languages were not restricted.

Study Appraisal and Synthesis Methods: The titles and abstracts collected from the electronic searches in those databases were evaluated. Then, the full-text versions of relevant studies were thoroughly assessed and extracted. The risk of bias was examined by using the Cochrane Collaboration's tool for assessing risk of bias. The primary efficacy of outcome was the pooled mean changed scores of the rating scales for Aberrant Behavior Checklist (ABC). However, the pooled response, overall discontinuation rate and discontinuation rate due to adverse events were also measured. Relative risks (RRs), and weighted mean differences (WMDs) or standardized mean differences (SMDs) with 95% confidence intervals (CIs) were estimated by using a random effect model.

Results: A total of 177 randomized subjects in three RCTs [1–3] were included in this review. The ABC rating scale was applied to evaluate symptoms of ASD in all RCTs. The pooled mean-changed score of ABC for irritability subscale in the risperidone-treated group was significantly higher than that of the placebo-treated group with WMD (95% CI) of −8.5(−11.99, −5.00), I2 = 62%. Additionally, the pooled mean-changed score of ABC for other subscales in the risperidone-treated group had also significantly greater than that of the placebo-treated group. Similarly, the pooled response of the risperidone-treated group was significantly greater that of the placebo-treated group with RRs (95% CI) of 2.57(1.35, 4.86), I2 = 77%. The pooled overall discontinuation rate and the discontinuation rate due to adverse events was not different between the two groups with RRs (95% CI) of 0.48(0.22, 1.06), I2 = 41% and (95% CI) of 0.72(0.23, 2.28), I2 = 0%, respectively.

Conclusions: Based on limited evidences, risperidone is efficacious in the treatment of ASD in children and adolescents. However, the acceptability and tolerability of this active agent were comparable to placebo. Therefore, the short term treatment of children and adolescents with ASD with risperidone may be beneficial. However, further well-defined study should be carried out to confirm these findings.

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Disclosure Statement: This abstract received financial support from Chiang Mai University, Thailand. NM has received travel reimbursement from Lundbeck and Pfizer. BM has received honoraria and/or travel reimbursement from Lundbeck and Pfizer. SL has received honoraria and/or travel reimbursement from Janssen-Cilag, Lundbeck, Daiichi Sankyo, and Pfizer. MS has received honoraria, consultancy fees, research grants, and/or travel reimbursement from AstraZeneca, GlaxoSmithKline, Pfizer, Janssen-Cilag, Johnson & Johnson, Lundbeck, Thai-Otsuka, Sanofi-Aventis, and Servier. SP, PW, and AM report no conflicts of interest in this work.

P.7.d.006 Methylphenidate long-term effects on psychiatric outcomes in a Sardinian ADHD population: preliminary results from the prospective ADDUCE project

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Background: Methylphenidate (MPH) is the most common first-line therapy for ADHD (Attention Deficit Hyperactivity Disorder) in Europe: many studies have examined its effectiveness and have shown a response rate of around 70%, with improvements seen in many areas (inattentiveness, impulsiveness and self-esteem) [1], though its long term safety is still controversial. The Attention Deficit Hyperactivity Disorder Drugs Use Chronic Effects (ADDUCE) project is an EU funded programme to evaluate the safety of MPH in the long term by systematic review of published information, data-mining from available databases and a large multi-national prospective study (WP 3). Using the Sardinian sample of the WP 3 ADDUCE sample we investigated the association between MPH and increased risk for psychiatric adverse effects after at least 1 year of treatment.

Objectives: To evaluate, within the prospective, longitudinal, pharmacovigilance, EU funded project ADDUCE, whether methylphenidate for ADHD is associated with a statistically significant increase in long-term risk of psychiatric effects (mood disorder, suicidal behaviour, psychotic symptoms and substance misuse). We further evaluated if the onset of psychiatric adverse effects correlate to the severity of ADHD and if the MPH use in the long term interferes on tic severity.

Methods: According to the ADDUCE protocol [2], psychiatric symptoms were assessed every six months for two consecutive years by the following scales: Mood and Feelings Questionnaire (MFQ) Short Version for child and parent; Psychosis Like Symptoms (PLikS); Columbia–Suicide Severity Rating Scale (C-SSRS); Substance Use Questionnaire (SUQ).

Results: One hundred and twenty-one ADHD Sardinian subjects (104 M; 17 F), aged 6–17, were enrolled and divided into two the following groups: 66 ADHD starting on MPH for the first time (ADHD-MPH+) and 55 untreated ADHD (ADHD-NO MPH). The two groups appeared to be comparable for ADHD subtype, cognitive functioning, age and gender distribution. A significative difference between the two groups was found for ADHD symptoms severity ($p = 0.001$) and the rate of comorbidities, particularly in relation to Oppositional Defiant Disorder (ODD; $p < .001$). Data from MFQ-child version, SUQ, Pliks, C-SSRS, have been analysed at two time points: baseline visit and after 24 months. 81 subjects (51 ADHD-MPH+ and 30 ADHD-NO MPH) completed the psychiatric assessment at 24 months visit. After 24 months we found a clinical trend for improvement on depressive symptoms measured by the MFQ-child version in both groups ($p = 0.001$ for ADHD-MPH+ and 0.007 for ADHD-NO MPH) and by the MFQ-parent version for the medicated group ($p = 0.04$). No significant differences were found for substance misuse, psychotic symptoms suicidal ideation and severity of tic after 24 months of treatment in the medicated group, resulting substantially comparable to the non medicated sample.

Discussion: Preliminary analysis on the present sample revealed that MPH is safe in the long term and could even help in managing depressive symptoms in the ADHD population improving the global functioning of patients. Firm conclusions on the efficacy and safety of medication on the psychiatric comorbid symptoms could be however drawn only when the total ADDUCE sample will be included in the analysis.

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Disclosure statement: This project has received funding from the European Union's Seventh Framework Programme for research, technological development and demonstration under grant agreement n. 324487.

P.7.d.007 A randomized, double blind, placebo-controlled, efficacy study of Omega 3/6 in children with mild to moderate inattentive ADHD – preliminary results

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Background: Attention Deficit Hyperactivity Disorder (ADHD) is a child psychiatric disorder characterized by inattention, hyperactivity and impulsivity with a significant global functional impairment. Treatment is based on behavioural and pharmacological approaches [1]. Recently there has been a growing interest in non pharmacological treatments, as dietary supplementation of omega-3/6 fatty acids, which seem to be deficient in ADHD individuals [2] and moderately effective in reducing inattentive symptoms [3].

Objectives: The primary objective was to evaluate the efficacy of a specific Omega-3/6 combination dietary supplement in a population of Italian children with predominantly Inattentive Type of ADHD (ADHD-I). The primary efficacy measure was the change from baseline of the ADHD Rating Scale (ADHD-RS-IV) score. The secondary objectives were to evaluate the efficacy of Omega3/6 supplement compared to placebo on global functioning and severity of illness by using respectively the Children-Global Assessment Scale (C-GAS), the Clinical Global Impression of Improvement (CGI-I) and the Clinical Global Impression-Severity (CGI-S). Depression and anxiety symptoms were also assessed by the CDRS-R (Children's Depression Rating Scale-Revised) and MASC (Multidimensional Anxiety Scale for Children).

Methods: The study was a randomised, double-blind, multicentre, placebo-controlled efficacy trial of Omega-3/6 combination in children aged 6 and 12 with mild to moderate ADHD-I, according to DSM-IV criteria. The study, conducted in 4 Italian sites (Cagliari, Roma, Pisa and Messina), included a screening and baseline assessment, a phase I double blind evaluation of Omega-3/6 supplement vs placebo (6 months) and a phase II open label treatment period of further 6 months during which all subject were on the Omega3/6 dietary supplement. Clinical assessments have been performed at 5 time points: baseline, 1 month, 3 months, 6 months and 12 months.

Results: 160 drug naïve ADHD Italian children (118 M; 42 F) were enrolled. 45 patients did not complete the study (drop out 28%). Preliminary results have been obtained by analysing scores at baseline visit and after 12 months. By this way, we included in the analysis both patients treated with active supplement for 12 months and patients treated openly with Omega3/6 supplement only for the last six months. Statistical significance was calculated by ANOVA for repeated measures. A significant effect at the end of the study ($p < 0.001$) was found for the following scales: ADHD-RS total score, ADHD-RS-Inattentive, CGI-S, CGI-I, CGAS. No significant changes were found for ADHD-RS-Hyperactivity and CDRS. Further analysis are in due course.

Discussion: Preliminary results suggest a significant improvement in global functioning and in ADHD symptoms severity, after at least 6 months of treatment with Omega-3/6 dietary supplementation. Omega-3/6 fatty acids resulted significantly effective

especially in reducing the inattention symptoms. Considering the limited choice of interventions for treatment in ADHD-I children, Omega-3/6 supplementation may offer a natural intervention to improve the quality of life of this population.

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Disclosure statement: The study was supported by an unrestricted grant from Vifor Pharma.

P.7.d.008 Perampanel treatment in drug-resistant focal epilepsy with de novo mutation CACNA1H: characteristics and clinical outcome

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Introduction: CACNA1H mutations, the gene encoding the T-type channels Cav3.2 calcium, localized on the chromosome 16p13.3, in several studies is detected in association with various forms of idiopathic generalized epilepsy. The T-type calcium channels play an essential roles in regulation of excitability and activation of neuronal networks [1] and network oscillations in the brain. A mutation of T-type calcium channels may influence neuronal excitability (causing an excessive neuronal activation) either by altering the biophysical properties of the channels or by increasing their surface expression. This abnormal condition may be modulated by antiepileptic drugs (AED), that could reduce the gateway of calcium positive ions on the postsynaptic membrane, restoring the balance of charges Ionian. An example of antiepileptic drug able to modulate the excessive neuronal activation is Perampanel. The Perapmanel is non-competitive AMPA glutamate antagonist receptor that in vitro inhibits the intracellular increase of positively charged ions, reducing the depolarization of the post-synaptic membrane [2].

Here we describe a case report of two patients (sisters) both with drug-resistant focal epilepsy and variant c.1546C > T heterozygous of the gene CACNA1H.

Methods: We identified a single nucleotide variant for a c.1546C > T heterozygous of the gene CACNA1H (chromosome 16p13.3) in two sisters aged 9 and 15 years with drug-resistant focal epilepsy.

These patients displayed multidaily focal seizures characterized by pavor, scream, extensor hypertonus of the upper and lower limbs, flushing. Several antiepileptic drugs have been tried with none or very poor results.

At the light of detected genetic mutation, Perampanel treatment has been started in add-on to Carbamazepine in both sisters (as off label for the second one).

Titration was started at 2mg per day and up-titrated to 8mg per day in both sisters, with a follow up of 2 years in the first-born and 6 months in the second-born.

During the follow-up, we conduced hematology and chemistry assessment, electrocardiography with QTc interval measurement, electroencephalogram and neuropsychological evaluations, at baseline and after 1 and 6 months.

Results: The seizure frequency has significantly decreased in both sisters, with complete resolution of symptoms in the first-born. Both sisters have presented some adverse effects, dose-dependent, like craving for food, headache, dizziness, asthenia and irritability, which resolved after fragmentation of the dose. Hematology and chemistry assessment and instrumental examinations have not shown abnormalities. No Severe Side Adverse Events (SAE) were reported.

Conclusions: From the analysis of this clinical cases, we can assume the efficacy of Perampanel as add-on for focal epilepsy drug-resistant associated with mutation of gene CACNA1H.

The mutation detected in our patients may be associated with a different a clinical phenotype, therefore, the genotype-phenotype correlation could be wider than literature detected [3].

Research and description of these cases could be useful for defining a more specific syndrome; furthermore, this case may underlie the importance of individualized genomic approach for treatment guidance in epilepsy.

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P.7.d.009 Perampanel treatment in early-onset epileptic encephalopathy with infantile movement disorders associated with de novo GRIN1 gene mutation

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Introduction: Early-onset epileptic encephalopathies (EOEE) encompass a group of severe disorders characterized by recurrent seizures and/or electroencephalographic abnormalities with progressive cerebral dysfunction [1]. Although a growing number of studies is providing new insights into the causal role of genes involved in synaptogenesis and neuronal circuitry, few data about individualized treatment options have been reported, so far. Here we describe a 5-years-old patient with EOEE with infantile movement disorder successfully treated with perampanel, with a 4-months-follow-up.

Methods: In setting up a multicenter whole exome sequencing (WES) analysis (Synaps study), we identified a single nucleotide variant for a c.1984A > T – p.Met662Leu in the GRIN1 gene (chromosome 9q34.3) in a 5-year-old girl with EOEE and infantile movement disorder. The patients displayed multidaily focal

frontiers in Psychiatry

ORIGINAL RESEARCH
published: 03 October 2017
doi: 10.3389/fpsyt.2017.00189

The Utility of a Computerized Algorithm Based on a Multi-Domain Profile of Measures for the Diagnosis of Attention Deficit/Hyperactivity Disorder

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OPEN ACCESS

Edited by:
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Specialty section:
This article was submitted to Child and Adolescent Psychiatry, a section of the journal Frontiers in Psychiatry

Received: 18 July 2017
Accepted: 14 September 2017
Published: 03 October 2017

Citation:
Crippa A, Salvatore C, Molteni E, Mauri M, Salandi A, Trabattoni S, Agostoni C, Molteni M, Nobile M and Castiglioni I (2017) The Utility of a Computerized Algorithm Based on a Multi-Domain Profile of Measures for the Diagnosis of Attention Deficit/Hyperactivity Disorder. Front. Psychiatry 8:189. doi: 10.3389/fpsyt.2017.00189

The current gold standard for diagnosis of attention deficit/hyperactivity disorder (ADHD) includes subjective measures, such as clinical interview, observation, and rating scales. The significant heterogeneity of ADHD symptoms represents a challenge for this assessment and could prevent an accurate diagnosis. The aim of this work was to investigate the ability of a multi-domain profile of measures, including blood fatty acid (FA) profiles, neuropsychological measures, and functional measures from near-infrared spectroscopy (fNIRS), to correctly recognize school-aged children with ADHD. To answer this question, we elaborated a supervised machine-learning method to accurately discriminate 22 children with ADHD from 22 children with typical development by means of the proposed profile of measures. To assess the performance of our classifier, we adopted a nested 10-fold cross validation, where the original dataset was split into 10 subsets of equal size, which were used repeatedly for training and testing. Each subset was used once for performance validation. Our method reached a maximum diagnostic accuracy of 81% through the combining of the predictive models trained on neuropsychological, FA profiles, and deoxygenated-hemoglobin features. With respect to the analysis of a single-domain dataset per time, the most discriminant neuropsychological features were measures of vigilance, focused and sustained attention, and cognitive flexibility; the most discriminating blood FAs were linoleic acid and the total amount of polyunsaturated fatty acids. Finally, with respect to the fNIRS data, we found a significant advantage of the deoxygenated-hemoglobin over the oxygenated-hemoglobin data in terms of predictive accuracy. These preliminary findings show the feasibility and applicability of our machine-learning method in correctly identifying children with ADHD based on multi-domain data. The present machine-learning classification approach might be helpful for supporting the clinical practice of diagnosing ADHD, even fostering a computer-aided diagnosis perspective.

Keywords: attention deficit/hyperactivity disorder, machine learning, support vector machines, near-infrared spectroscopy, fatty acids

INTRODUCTION

Attention deficit/hyperactivity disorder (ADHD) is among the most common neurodevelopmental disorders, affecting 7.2% of children worldwide (1), with a significant impact on familial, relational, and school functioning in more than one setting. ADHD is a highly heterogeneous condition with manifold causes, progressions and a broad range of symptom manifestations. The diagnostic criteria for ADHD include purely behavioral descriptions of symptoms, which often overlap with the manifestations of many other psychopathologies. Currently, despite the fact that brain structural and functional deficits have been proven in subjects with ADHD, the gold standard for diagnosis consists of subjective measures, such as a clinical interview, observation, and rating scales. These procedures are long term and are heavily based on experiences and practical knowledge of clinicians. The limited reliability of this assessment has led to diagnostic variability across different clinicians and cultures (2). This also contributes to social concerns about the possible harms of misdiagnosing (3, 4).

For these reasons, the diagnosis of ADHD still represents a challenge, and clinicians highly demand the availability of more objective and reliable measures for diagnosing subjects with ADHD. Recent studies have explored the value of behavioral as well as neurophysiological measures for automatically discriminating between children with ADHD and typically developing (TD) peers, possibly fostering a computer-aided diagnosis perspective. These studies typically make use of machine-learning algorithms to distinguish the subjects of different groups by maximizing the distance between datasets. Machine learning commonly refers to all procedures that train a computer algorithm to automatically extract meaningful information from the data and to use it to make predictions about the group membership of new individuals (e.g., patients vs. controls). Machine-learning methods are multivariate analysis methods that also offer the advantage of identifying complex patterns of differences that univariate statistical methods do not efficiently recognize. Thus, the use of these methods should not be simply considered a potential "diagnostic" tool but also a useful procedure for identifying objective measures at an individual level from a larger dataset to be used for single-subject diagnosis. A number of studies recently indicated that the machine-learning classification approach may lead clinicians toward an efficient and accurate diagnosis of ADHD using behavioral/cognitive measures (5) or neurophysiological techniques, such as electroencephalography (6), structural magnetic resonance imaging (MRI) (7), and resting-state functional MRI (8).

In this work, we developed a supervised machine-learning method to recognize school-age children with ADHD and to correctly separate them from TD peers, by using, for the first time, a multi-domain dataset comprising blood fatty acid (FA) profiles, neuropsychological measures, and functional measures obtained from near-infrared spectroscopy (fNIRS). We included these measures based on both the extant literature and on our previous findings. With respect to blood FAs, we followed the suggestion that polyunsaturated fatty acids (PUFAs) shortage could be one of the various etiological factors of ADHD (9), and we recently reported an abnormal FA profile in children with ADHD (10). Furthermore, given the abovementioned work of Bledsoe and colleagues (5) that applied pattern classification methods to behavioral/cognitive measures with promising results, we included the neuropsychological tests of vigilance, attention, and flexibility. Because some debate has occurred in the literature over the use of neuropsychological tests for the diagnosis of ADHD, we were interested in understanding in the present wok the possible predictive value for these measures. Indeed, it was suggested that no psychometric test can be used with confidence for the purposes of diagnostic decision (11, 12) and previous studies demonstrated low to moderate correlations between scores on these tests and other assessment measures for ADHD (13, 14). Finally, such tests do not correlate significantly with parent and teacher ratings of executive functioning (EF) in the child's daily life activities (15). However, it is worth mentioning that more "ecological" measures of EF could describe different cognitive profiles in children with ADHD-only, ADHD and comorbid disorders, and healthy controls, with a good correlation with parent ratings of EF in everyday activities (16). Finally, we introduced a non-invasive method of functional neuroimaging, fNIRS, to measure the hemodynamic responses to neuronal activation during a spatial working memory task. Near-infrared spectroscopy (NIRS) was chosen among the neuroimaging techniques because it imposes fewer environmental constraints, and due to the low cost of scanning. In addition, previous evidence showed that NIRS could be useful for identifying children with ADHD (17, 18). We included, as stimulation paradigm, a visuospatial *N*-back working memory task consisting of three tasks with increasing difficulty: baseline, 1-back, and 2-back. The choice of such a task was based on the suggestion that a deficit in working memory could be a core cognitive impairment of ADHD (19).

Given that the ADHD etiology is generally considered multifactorial, our hypothesis was that the integration of information from the different sources and levels of analysis would lead to a significantly more effective identification of children with ADHD, compared with using a single-domain dataset per time. Indeed, following a multifactorial etiological model, the emergence of the disorder could be related to the simultaneous malfunction of mechanisms interacting at multiple levels, with each resulting in a different degree of impairment across children. Moreover, our method could support the clinicians' decision on the tests to be included in the ADHD diagnostic process. In fact, as Kim and colleagues (20) recently proposed in their study predicting

Abbreviations: PUFA, polyunsaturated fatty acid; TD, typically developing children; DSM-IV TR, Diagnostic and Statistical Manual of Mental Disorders Fourth edition, text revised; DAWBA, Development and Well-Being Assessment; FSIQ, Full Scale Intelligence Quotient; ANT, Amsterdam Neuropsychological Tasks; FA, fatty acid; AA, arachidonic acid; EPA, eicosapentaenoic acid; DHA, docosahexaenoic acid; SFA, saturated fatty acid; MUFA, monosaturated fatty acid; C, control; 1B, 1-back; 2B, 2-back; F, frontal; Oxy-Hb, oxygenated-hemoglobin; Deoxy-Hb, deoxygenated-hemoglobin; PCA, principal components analysis; FDR, Fisher's discriminant ratio; NPS, neuropsychological features; BIO, fatty acid profile features; NIRS OXY, Oxy-Hb NIRS features; NIRS DEOXY, Deoxy-Hb NIRS features; CV, cross validation; RT, reaction time; AUC, area under the curve; SVM, support vector machine; BOLD, blood oxygenation level dependent.

methylphenidate response in ADHD *via* the machine-learning approach, we could investigate whether the use of several measures is worth the additional costs of collecting more data, based on any increase in the classification accuracy.

MATERIALS AND METHODS

Participants

Twenty-two children with ADHD were compared with 22 TD children matched by gender, age, and intelligence quotient (IQ). All participants in the clinical group were previously diagnosed according to the Diagnostic and Statistical Manual of Mental Disorders Fourth Edition, text revised (DSM-IV TR) (21) criteria by a medical doctor specialized in child neuropsychiatry with expertise in ADHD (Antonio Salandi and Sara Trabattoni). A child psychologist (Alessandro Crippa) confirmed independently the clinical diagnoses using the semi-structured interview Development and Well-Being Assessment (DAWBA) (22). According to interviews, 18.2% of children in the ADHD group met criteria for the inattentive subtype, 36.4% met criteria for the hyperactive–impulsive subtype, and 45.5% met criteria for the combined subtype. The TD group consisted of children recruited by local pediatricians and from schools in the vicinity of our institute, with no history of medication treatment. Signs of social/communicative disorders and other possible DSM-IV TR diagnoses were excluded in TD children through the administration of the DAWBA interview to parents. To match the two groups, the estimated Full Scale Intelligence Quotient (FSIQ) was measured in TD participants using the Block Design and Vocabulary subtests of the Wechsler Intelligence Scale for Children—III (WISC-III) (23). These two WISC subtests have a correlation of 0.93–095 with the FSIQ (24). Children in both groups were required to have FSIQ or estimated FSIQ scores of higher than 80 on the WISC-III or WISC-IV scales (23, 25). All participants were Caucasian, had normal or corrected-to-normal vision, and were not taking any medication. The study was explained to both children and their parent(s) or caregivers, and all of the participants' legal guardians signed the informed written consent before the children's participation. The research received approval from the ethic committee of our institute and was therefore performed in accordance with the ethical standards set forth in the 1964 Declaration of Helsinki and its later amendments.

Measures

Cognitive Profile

The executive function profile of each participant was assessed through a selected battery of cognitive tests from the Amsterdam Neuropsychological Tasks (26). All children completed four computerized tasks, administered in the following order: Baseline speed, Focused attention four letters, Shifting attentional set–visual, and Sustained attention. Baseline speed consisted of a simple reaction time (RT) task. During the Focused attention test, participants had to selectively respond to one target letter among four, when it was presented in the relevant diagonal position, and to ignore it when it was displayed in the irrelevant axis. The Visual set-shifting task was used to investigate three different cognitive dimensions: vigilance, inhibition, and cognitive flexibility. Finally, the Sustained attention was used to assess the fluctuation of attention over time. For further details about the dependent measures considered for these tasks, see Crippa et al. (10).

FA Profile

Blood samples were taken from all participants to assess the FA profiles. Samples of blood were directly subjected to transmethylation for gas chromatography analysis, using a well-validated protocol (27). FAs from 14 to 24 carbons were detected. In this study, we reported the percentages of single FAs only for main omega-3 and omega-6. Furthermore, we calculated ratios as arachidonic acid (AA)/eicosapentaenoic acid (EPA) and AA/docosahexaenoic acid (DHA), as they have been pointed out as reliable indexes of the functional effects of long-chain PUFAs (28). Finally, we calculated the sum of EPA and DHA (the "omega-3 index") (29), and of saturated fatty acid (SFA), monounsaturated fatty acid (MUFA), and PUFA. For further details about the FA profile analysis, see Crippa et al. (10).

Features accounting for both the cognitive and the FA profiles were Z-scored according to $z_i = (x_i - m_x)/s_x$, where x_i is the value of a given feature x for the ith subject, m_x and s_x are the mean value and the SD, respectively, of feature x over the considered population, and z_i is the resulting Z-scored feature.

Neurophysiological Profile

Stimulation Protocol

The stimulation protocol was developed with the Presentation® software (Neurobehavioral Systems Inc.), and stimuli were displayed using a computer screen. The task was a modified version of the visuospatial *N*-back working memory task that Cui and colleagues (30) set up and that lasted approximately 15 min. The paradigm consisted of three tasks—control (C), 1-back (1B), and 2-back (2B)—always presented in this order: rest–C–1B–2B–rest–1B–C–2B–rest–2B–1B–C–rest. The first rest epoch was 60 s long, and the other three rests were 30 s long. During the rest, children passively viewed an image on a black screen. Experimental epochs began with a 3 s display of the instruction: "Repeat" in the 1-back task and "Return" in the 2-back task. Control epochs each began with a 2-s display of the instruction, "Center." Each control and experimental epoch included 32 stimuli shown for 0.5 s each, with a 1.5 s interstimulus interval. The stimulus was a clown's face displayed in one of nine locations in a 3 × 3 matrix. In the 1-back task, children were required to respond if the stimulus remained in the same position of the previous trial ("Repeat"). In the 2-back task, participants had to respond whether the stimulus recurred in the same location as it did in the two previous trials ("Return"). In the control task, children were instructed to respond only when the clown's face was presented in the center of the screen. Practice trials, the number of which varied individually, were given to participants before NIRS recording.

NIRS Data Acquisition and Optode Localization

A commercial continuous wave NIRS device (DYNOT Compact, NIRxBerlin) was employed for NIRS recordings. An elastic cap of the proper head size was fitted on the subject's head. The cap

had 32 channels, with 8 emitters and 24 detectors; it was placed on the child's scalp at the bilateral frontotemporal areas, centered at F3 and F4 according to the International 10–20 system (31), as shown in **Figure 1**.

Near-infrared spectroscopy recording was performed at two wave lengths (760 and 830 nm) to probe oxygenated-hemoglobin and deoxygenated-hemoglobin (Deoxy-Hb), respectively, in the brain. The measurement principles were based on the modified Beer–Lambert law, for which oxygenated-hemoglobin and Deoxy-Hb changes are calculated from the change in light attenuation at a given measured point (32).

NIRS Preprocessing

First, we visually inspected individual NIRS data to remove obvious artifacts; then, we filtered the signals with a low-pass filter at 0.3 Hz, to respect the task/rest frequency that the stimulation protocol induced. Continuous signals were then divided into epochs starting 14 s before the onset of each task block, and ending 14 s after the end of the blocks. In doing so, nine epochs, lasting 92 s each, were extracted. Epochs were first averaged on the basis of the stimulation type (C, 1B, and 2B) and then grouped, to obtain a grand average. Because the raw NIRS data represented relative values and could not be directly compared across subject or channels, we standardized the raw data into *Z*-scores based on a "baseline" period immediately ahead of the task epoch. In this manner, we could depict the relative change in oxygenated-hemoglobin and Deoxy-Hb concentrations that the visuospatial *N*-back working memory task induced. As Ichikawa and colleagues (11) previously suggested, we selected as "baseline" for standardizing the raw data a period of 3 s just before the beginning of each stimulation period. The *Z*-scores were calculated for each subject *i* using the following formula:

$$z_i = (x_{i,\text{task}} - m_{i,\text{baseline}}) / s_{i,\text{baseline}}, \quad (1)$$

where $x_{i,\text{task}}$ is the raw data (mM mm) of the *i*th subject at each time point during the task period and $m_{i,\text{baseline}}$ and $s_{i,\text{baseline}}$ are the mean value and the SD, respectively, of the raw data of the *i*th subject during the baseline period.

Data Analysis

First, data were visually and statistically inspected to verify that the assumptions were not violated. A chi-square analysis was then carried out to assess group differences in gender distribution and fish consumption. An independent-samples t test was used to individually examine group differences in age, IQ, and socioeconomic status. The alpha level was set to 0.05 for all data analyses.

Feature Extraction and Selection

To reduce the features to the most relevant ones for the classification, we performed feature extraction and selection on *Z*-scored data. Feature extraction and selection were applied only to NIRS data.

Feature extraction was performed through principal components analysis (PCA) (33), a technique that has been widely used in the literature across different automatic-classification tasks (34). PCA is able to extract a smaller set of features from the original set of observed data, with these features being referred to as PCA coefficients. PCA coefficients are uncorrelated and sorted according to the maximum-explained-variance criterion.

Extracted PCA coefficients were then ranked according to their Fisher's discriminant ratios (FDRs); the FDR is an index that measures the binary-class discriminatory power for each feature as follows:

$$\text{FDR} = \frac{(\mu_{\text{ADHD}} - \mu_{\text{TD}})^2}{\sigma^2_{\text{ADHD}} + \sigma^2_{\text{TD}}}, \quad (2)$$

where μ and σ are the mean and the variance, respectively, of the given feature on the whole ADHD or TD dataset. The top 60% PCA coefficients with the highest FDRs were selected and retained for automatic classification.

The Classifier

A support vector machine (SVM) (35) was used to automatically classify ADHD and TD.

Support vector machines are machine-learning algorithms that able to (1) generate a predictive model by learning how to separate a set of binary-labeled data, called a training set, and

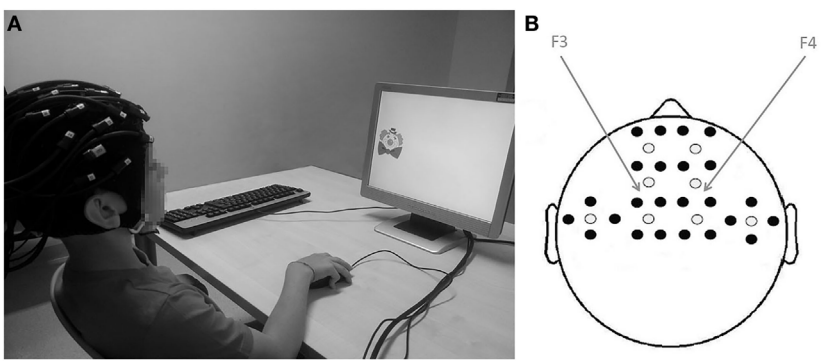

FIGURE 1 | **(A)** Brain activity was measured while participants performed the visuospatial *N*-back working memory task; **(B)** from near-infrared spectroscopy measurements. Location of sources (white dots) and detectors (black dots). The fibers were placed on the bilateral frontotemporal areas centered at F3 and F4 according to the International 10–20 system. The distance between the fibers was set at 2.7 cm.

(2) use this predictive model to automatically classify unlabeled data in one of the two classes of the training set (in our case, ADHD and TD). The training set consists of (1) a matrix of samples belonging to two different classes, with each sample being represented by a set of selected features, and (2) the corresponding vector of binary labels. Automatic classification was performed using the following features individually: neuropsychological features accounting for the cognitive profile (NPS), features accounting for the FA profile (BIO), features obtained from the oxygenated-hemoglobin NIRS spectra (NIRS OXY), and features obtained from the Deoxy-Hb NIRS spectra (NIRS DEOXY). A classification using NIRS OXY and NIRS DEOXY data taken together was also performed. For each subject, the clinical diagnosis (ADHD and TD) was used as a label for the training of the classifier. The classification system was previously validated in a clinical setting (36). Because we chose to employ a linear kernel (which ensures better computational efficiency in comparison to other kernels), we did not perform any optimization of the SVM regularization hyper parameter.

Optimization of Features and Performance Evaluation

To find the optimal combination of features for the automatic-classification task, we used a wrapper approach, in which optimization is seen as a search problem. Specifically, different combinations of features were prepared, evaluated through the machine-learning classifier, and assigned a score based on model accuracy. Once all combinations of features were evaluated, the optimal combination was chosen as the one able to return the highest accuracy of classification.

The optimization of features and performance evaluation were accomplished through a nested 10-fold cross validation (nested CV). The original dataset was split into 10 subsets of (possibly) equal size. Nine out of 10 subsets were used in an inner loop to perform the optimization of features, and the held-out subset was used in an outer loop to evaluate the performance of the classification of the optimal combination of features. This process was repeated 10 times, to use all subsets once for performance evaluation. For each of the 10 rounds, the accuracy, sensitivity, and specificity of classification in the outer loop were evaluated, and the results were averaged across all rounds. The flowchart of the nested CV of the proposed machine-learning method for the NIRS features is depicted in **Figure 2A** as a representative example.

For cognitive and FA profile data, we were interested in determining which features were the most important for the classification. As mentioned earlier, for each of the 10 rounds of the nested CV, we obtained an optimal combination of features from the inner loop. The importance of features for classification was defined as the occurrence frequency of each feature in the optimal combinations.

Ensemble of Classifiers

To improve the performance of the single classification systems, we designed an ensemble of classifiers by combining the different predictive models mentioned earlier. Specifically, we trained four different classifiers on independent datasets (NPS features, BIO features, NIRS OXY features, and NIRS DEOXY features, respectively) thus obtaining four independent predictive models, namely the "Predictive model #1" trained on NPS features, the "Predictive model #2" trained on BIO features, the "Predictive model #3" trained on NIRS OXY features, and the "Predictive model #4" trained on NIRS DEOXY features. The predicted outputs were then combined through the majority-vote rule. This procedure allowed us to examine whether the decision of including any additional measure along the diagnostic process is worth the costs, based on any increase in the classification accuracy. Accordingly, given a new (unlabeled) subject, each binary classifier predicts a label for that subject, corresponding to a class. Predicted labels of each binary classifier are then treated as votes for the corresponding class, and the class with the largest number of votes is chosen as the class that the ensemble predicts. A flowchart illustrating this approach is depicted in **Figure 2B**. The ensemble of classifiers was obtained through the combination of three or four of these predictive models, which led to the following ensembles:

1. NPS + BIO + NIRS OXY
2. NPS + BIO + NIRS DEOXY
3. NPS + NIRS OXY + NIRS DEOXY
4. BIO + NIRS OXY + NIRS DEOXY
5. NPS + BIO + NIRS OXY + NIRS DEOXY

Finally, the proposed classification algorithm was translated into a final software tool that could allow clinicians, by means of a graphic interface, to upload the profile of measures collected from each patient/participant (the blood FA profile, the neuropsychological measures, and the fNIRS spectrum) and to obtain an automatically predicted diagnosis.

RESULTS

Participants and Measures

Data on the demographic characteristics of the participants are summarized in **Table 1**. The statistical analyses confirmed the validity of gender, age, and full-scale IQ matching (all $p > 0.05$). Further, socioeconomic status and weekly fish consumption as referred to by parents were also balanced between groups (both $p > 0.05$).

Feature Extraction and Selection

This process was applied only to NIRS data. Feature extraction through PCA resulted in the extraction of $N - 1$ PCA coefficients, where N is the number of subjects in the *training* set ($N = 20$ or 21 depending on the particular round of the 10-fold nested CV).

Extracted PCA coefficients were then ranked according to their FDRs. The top 60% (i.e., 12) PCA coefficients with the highest FDRs were selected and retained for automatic classification.

Optimization of Features and Performance Evaluation

Retained features were fed into the 10-fold nested-CV process for optimization and performance evaluation. Specifically, all NPS

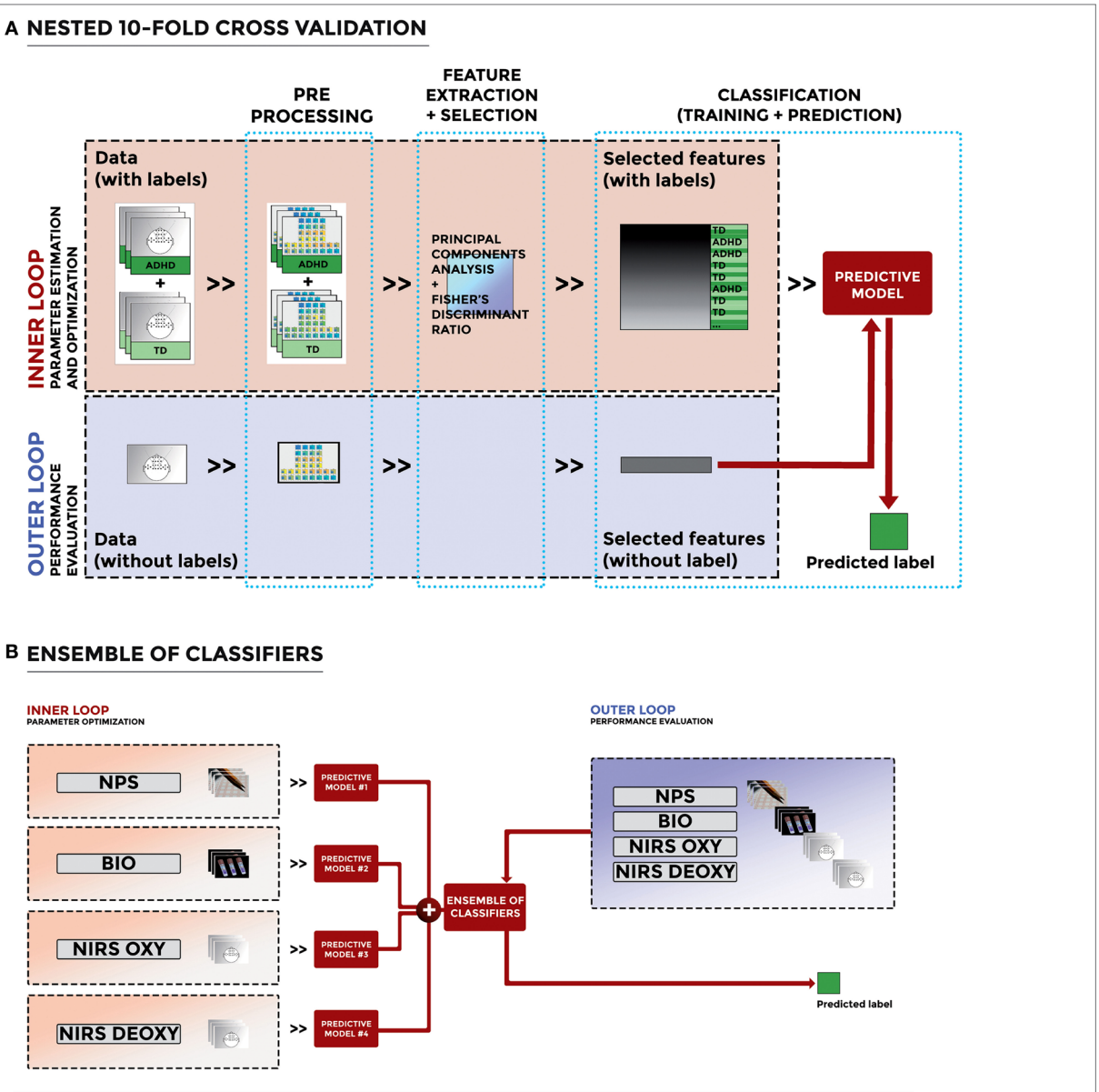

FIGURE 2 | **(A)** Flowchart of the nested cross validation of the proposed machine-learning method for the near-infrared spectroscopy (NIRS) features (as a representative example). The figure shows the different steps of our method, including preprocessing, feature extraction and selection, and classification. **(B)** Flowchart of the ensemble-of-classifiers approach applied to NPS, BIO, and NIRS data.

TABLE 1 | Sociodemographic characteristics of the participants.

	ADHD	TD		*p*
N	22	22		
Females:males	0:22	1:21	1.023[a]	0.312
Age	11.5 ± 1.5	11.4 ± 1.9	−0.220[b]	0.827
IQ	102.7 ± 11.1	109.6 ± 19.5	1.453[b]	0.154
SES	53.2 ± 20.6	56.1 ± 18.3	0.504[b]	0.617

ADHD, children with attention deficit/hyperactivity disorder (ADHD); TD, typically developing children; SES, socio economic status; IQ, intelligence quotient.
[a]*Chi-square test.*
[b]*Student's t-test.*

(18) and BIO (10) features were used, whereas NIRS features (both NIRS OXY and NIRS DEOXY) were reduced to 12 after feature extraction and selection. Considering that the process was used to evaluate all possible combinations of features, the number of evaluated combinations was as follows:

- NPS: 18 features → 2.6×10^5 combinations
- BIO: 10 features → 1,023 combinations
- NIRS: 12 features → 4,095 combinations

The performances of the machine-learning method for automatically classifying ADHD versus TD are reported in **Table 2**.

Classification was performed using NPS, BIO, NIRS OXY, and NIRS DEOXY features taken individually, as well as NIRS OXY and NIRS DEOXY features taken together. The classification accuracy reached a maximum of 78% (sensitivity 72%, specificity 82%) using NIRS DEOXY features. When using NPS or BIO features taken individually, accuracy resulted in 62 and 66%, respectively.

Besides calculating the performance for the automatic classification of ADHD versus TD, for neuropsychological and biological data, we were interested in determining which features occurred the most in the optimal combinations across the 10 rounds of the nested CV. This provided information about the importance of each feature for the classification. The most discriminant NPS features between the two groups, ranked by occurrence frequency in the optimal combinations, are reported here in descending order: Sustained attention–False alarms, Visual set-shifting–RT inhibition, Sustained attention–Coefficient of variation, Visual set-shifting–Number of inhibition errors, Focused attention–RT correct responses, Focused Attention–Correct rejections target non-relevant positon, Focused attention–SD of correct responses RT, Focused attention–Misses, Sustained attention–Misses, Baseline speed–SD of RT, Visual set-shifting–Number of errors flexibility, Sustained attention–Tempo × Series, Sustained attention–SD, Baseline speed–RT, Focused attention–Correct rejections non-target relevant position, Focused attention–False alarms target non-relevant position, Focused attention–False alarms irrelevant target, Visual set-shifting–RT flexibility. The most discriminant BIO features between the two groups, ranked by occurrence frequency in the optimal combinations, were in descending order: linoleic acid, PUFA, AA, EPA, omega-3 index, AA/DHA, AA/EPA, and MUFA. DHA and SFA were never selected as optimal discriminant features.

TABLE 2 | Performance of the machine-learning method (accuracy, sensitivity, and specificity) in the automatic classification of attention deficit/hyperactivity disorder vs. typically developing.

Features	Accuracy (mean ± SD)	Sensitivity (mean ± SD)	Specificity (mean ± SD)
NPS	62 ± 17	70 ± 27	57 ± 24
BIO	66 ± 21	58 ± 40	73 ± 29
NIRS OXY	57 ± 27	48 ± 47	67 ± 33
NIRS DEOXY	78 ± 22	72 ± 34	82 ± 24
NIRS OXY + NIRS DEOXY	72 ± 32	73 ± 29	68 ± 43

Classification was performed for cognitive profile (NPS), fatty acid profile (BIO), features obtained from the oxygenated-hemoglobin NIRS spectra (NIRS OXY), and features obtained from the deoxygenated-hemoglobin NIRS spectra (NIRS DEOXY) taken individually, or NIRS OXY and NIRS DEOXY features taken together. Values of mean and SD were calculated across all the possible folds and round of the cross validation process.

Ensemble of Classifiers

The performances of the ensemble of classifiers for automatically classifying ADHD vs. TD are reported in **Table 3**. The classification accuracy reached a maximum of 81% [sensitivity 73%, specificity 87%, area under the curve (AUC) 0.80] by combining the predictive models trained on the NPS, BIO, and NIRS DEOXY features. The ensemble of classifiers obtained combining the predictive models trained on the NPS, BIO, NIRS OXY, and NIRS DEOXY features resulted in an accuracy of 76% (sensitivity 83%, specificity 68%, AUC 0.75).

In **Figure 3A**, a screenshot of the graphic interface developed for a possible clinical use of the proposed method is shown. Specifically, as it can be seen, the tool allows one to upload the required data *via* a user-friendly interface. Required data are the blood FA profile, the neuropsychological measures, and the fNIRS spectrum of the single patient. After the data are uploaded, the results of the automatic single-subject classification are shown in a new screen, together with some notes about the clinical use of the tool and the privacy (**Figure 3B**).

DISCUSSION

In the actual practice, ADHD is diagnosed on the basis of symptoms as judged by clinicians and using qualitative measures, such as a structured interview, rating scales, and neuropsychological tests. The vast heterogeneity of ADHD manifestations represents a challenge for this assessment, potentially leading to misdiagnosis. The goal of this work was to investigate the ability of a multi-domain dataset, including blood FA profiles, neuropsychological measures, and fNIRS measures, to automatically discriminate school-aged children with ADHD from TD peers. To achieve this purpose, we applied for the first time, to our knowledge, a supervised machine-learning method for the analysis of biological, cognitive, and neurophysiological data together to identify children with ADHD. We hypothesized that the integration of information between different levels would increase the classification accuracy of ADHD, as compared with using a single-domain dataset per time. Moreover, we were interested in understanding whether our method could aid in the clinician's decision about which tests to include in the diagnostic process, based on the trade-off "increase of accuracy/cost."

With respect to the analysis of a single-domain dataset per time, our machine-learning method reached the lowest

TABLE 3 | Performance of the ensemble of classifiers [accuracy, sensitivity, specificity, and area under the curve (AUC)] in the automatic classification of attention deficit/hyperactivity disorder vs. typically developing.

Features				Accuracy (mean ± SD)	Sensitivity (mean ± SD)	Specificity (mean ± SD)	AUC
NPS+	BIO+	NIRS OXY		71 ± 10	70 ± 27	73 ± 24	0.70
NPS+	BIO+		NIRS DEOXY	81 ± 15	73 ± 24	87 ± 22	0.80
NPS+		NIRS OXY+	NIRS DEOXY	78 ± 18	70 ± 36	87 ± 22	0.77
	BIO+	NIRS OXY+	NIRS DEOXY	77 ± 21	63 ± 31	90 ± 21	0.77
NPS+	BIO+	NIRS OXY+	NIRS DEOXY	76 ± 16	83 ± 22	68 ± 23	0.75

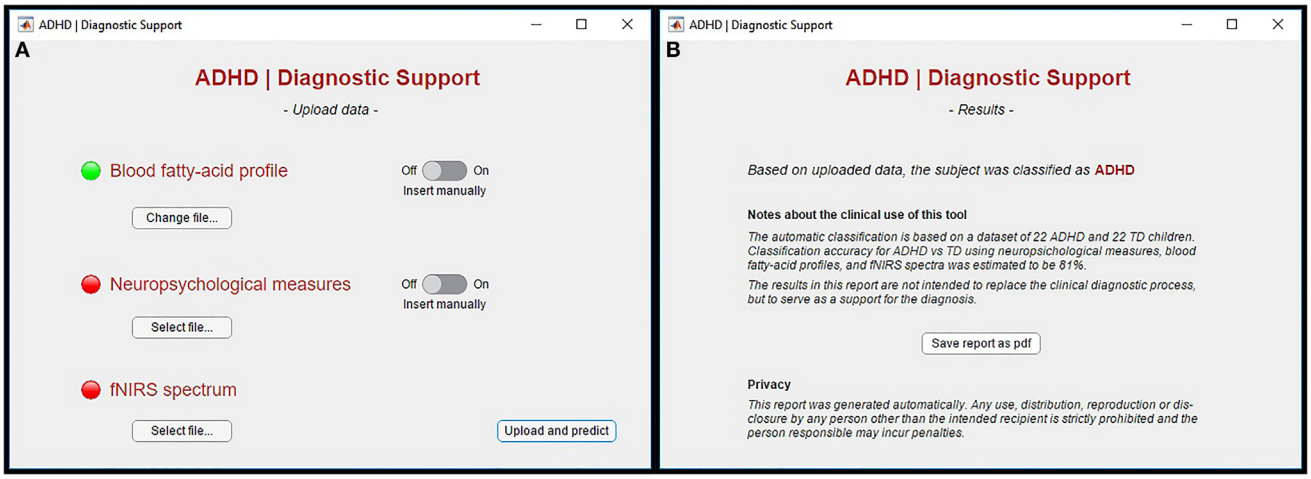

FIGURE 3 | **(A)** Screenshot of the graphic interface developed for the clinical use of the proposed machine-learning method. The tool allows one to upload the expected data *via* a user-friendly interface. Required data are the blood fatty-acid profile, the neuropsychological measures, and the from near-infrared spectroscopy (fNIRS) spectrum of the single patient. **(B)** After uploading the data, the results of the automatic single-subject classification are shown in a new screen, together with some notes about the clinical use of the tool and the privacy.

individual classification (62%), in the comparisons between children with ADHD and healthy controls, using the neuropsychological data derived from tests of vigilance, focused and sustained attention, and cognitive flexibility. This result was not directly comparable with the previous findings of Bledsoe et al. (5), as the best accuracy reached by the authors and derived from an SVM method also included the behavioral measures of ADHD symptoms, along with the measure of sustained selective attention. Nevertheless, the present result extends the previous findings, suggesting a possible executive/cognitive dysfunction in only 35–50% of children with ADHD (37), and supporting the claim no cognitive test at this time can be used with confidence for diagnostic decision by itself (11, 12). Moreover, the neuropsychological measures that were used to best predict ADHD in our study—false alarms and the intra-subject variability of responses during a sustained attention task, the number of errors, and the response time in a test assessing cognitive inhibition—are among the most frequently reported core cognitive features of ADHD (38, 39). The accuracy of our machine-learning method slightly improved (67%) when we included blood FA values only. Even though the level of classification was still moderate, we believe that this finding could be quite promising if confirmed with larger sample, given the fact that the procedure for collecting these data was fast and minimally invasive and could offer insight on the possible biological signature of ADHD. The present results extend the previous findings of abnormal FA percentages reported in a recent meta-analysis (40), and our previous findings from a clinical study involving a school-aged sample of children with ADHD (10). The FAs that are used to best identify ADHD seem to be linoleic acid, AA, EPA, EPA + DHA, and the total amount of PUFA. All of these components were extensively linked to ADHD in previous studies (40, 41). Our machine-learning method reached greater accuracy (72%) when we used, as a single-domain dataset, the cerebral hemodynamic responses (both oxygenated hemoglobin and deoxygenated hemoglobin) measured by NIRS during a spatial working memory task. Moreover, we achieved an even better accuracy of 78% when we considered only deoxygenated hemoglobin. The classification accuracy that was achieved in this study is nearly consistent with previous SVM applications to fNIRS data (17) or with conservative receiver operating characteristic analysis of fNIRS signal (18). Interestingly, we found a significant advantage of the deoxygenated-hemoglobin over the oxygenated-hemoglobin data (78 vs. 57%) in terms of classification accuracy. The deoxygenated-hemoglobin variation following local neural activation tends to be of a smaller amplitude compared with the oxygenated-hemoglobin response, but it seems to be a more reliable indicator of neural activity, less prone to inference by extra-cerebral physiological noise, and more correlated with the blood oxygenation level dependent signal (42–44). However, this issue is still controversial, with some other works suggesting higher retest reliability for oxygenated hemoglobin (45).

Beyond this, the point of relevance of our work was that, for the first time, we applied a machine-learning approach using biological, cognitive, and neurophysiological data together for automatically classifying children with ADHD. Our ensemble of classifiers reached an accuracy of 76% when we combined the predictive models trained on the whole multi-domain dataset. The classification accuracy of the ensemble reached a maximum of 81% through the combining of the predictive models trained on neuropsychological, FA profiles, and deoxygenated-hemoglobin features. Thus, the present findings clearly show the feasibility and applicability of machine-learning methods in correctly identifying children with ADHD on the basis of multi-domain data. Furthermore, the classification accuracy we reached, using the whole dataset, is consistent with the SVM application of Kim and colleagues (20) to a rich multi-domain dataset (including demographic, clinical, environmental, neuropsychological, neuroimaging and genetic

information) to predict the methylphenidate response in ADHD. The performance of the ensemble of classifiers only partially supported our initial hypothesis—i.e., integrating information from different domains would significantly increase the predictive value of our classification approach—as the analysis of the whole dataset minimally improved the classification accuracy (81% for the whole dataset vs. 78% using only NIRS DEOXY signal). Taken together, the results of the ensemble of classifiers clearly showed how the addition of deoxygenated-hemoglobin features increased the accuracy (from 71 to 76–81%). For this reason, we feel that the present findings do not support the decision of including all of the tests we used in a possible diagnostic assessment, on the basis of a gain of accuracy/cost trade-off. In particular, when we considered one domain at a time, we found a limited predictive value for the neuropsychological measures. On the contrary, the significant predictive value of our SVM classification approach of fNIRS data might be valuable for supporting the practice of diagnosing ADHD, even encouraging an fNIRS-based clinical diagnosis at an individual level. Indeed, two other recent studies showed the fNIRS feasibility in identifying children with ADHD with different methodological approaches (17, 18). Moreover, NIRS scanning is relatively low cost. It is also particularly favorable for measuring task-related neural activation in children with ADHD because NIRS requires less stabilization than other neuroimaging techniques do.

Despite our promising results, this study did have some limitations. The first one was that the sample sizes of participant groups were relatively small. To validate the proposed classification approach, we need to replicate the present findings with larger sample sizes so that we can test the computerized algorithm with a totally independent dataset. Another possible limitation of this work was that our classification algorithm was obviously specific to the sample used in training the classifier (i.e., school-aged children with ADHD), so the present findings could not be generalized to adult patients with ADHD. Moreover, future extensions of this study should test the disorder specificity of the classifier, including also other neurodevelopmental conditions frequently associated or in differential diagnosis with ADHD. Keeping these limitations in mind, we clearly emphasize that the proposed technique should not be considered a potential ADHD marker at this time. Indeed, no automatic algorithm can substitute clinical diagnostic decisions based on data from several informants regarding the child's everyday behavior in different settings. Therefore, in the actual clinical practice, our method should be considered only a complementary and adjunctive one to existent assessment measures. However, the abovementioned limitations should not prevent further investigations using the present approach. In this direction, given the spatial information that NIRS provides, it would be of interest to develop and refine our method to identify which brain regions specifically contribute to the predictive value of the classification.

In conclusion, we have provided preliminary evidence that school-aged children with ADHD can reliably be identified using a multi-domain dataset including blood FA profiles, neuropsychological measures, and fNIRS. The significant predictive value of the present machine-learning classification approach might be helpful for supporting the clinical practice of diagnosing ADHD, even fostering a computer-aided diagnosis perspective.

ETHICS STATEMENT

The study was explained to both children and their parent(s) or caregivers, and all of the participants' legal guardians gave their informed written consent before the children's participation. The research was approved by the Ethic Committee of our Institute and has therefore been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki and its later amendments.

AUTHOR CONTRIBUTIONS

AC, CS, MMolteni, MN, and IC conceived, designed, and drafted this work; EM conceived and designed the fNIRS paradigm; AS, ST, AC and MMauri performed the clinical and experimental evaluation of all participants; CA critically revised the method for fatty acids' analysis; all authors critically revised, and approved the final version of and agreed to be accountable for this work.

ACKNOWLEDGMENTS

The authors are especially grateful to all the families of the children who took part in this study.

FUNDING

This research was partially supported by grants from Dietetic Metabolic Food srl and from the Italian Ministry of Health to MN (RC 2015–2016, IGLOO) and by the Fund for Research of the Italian Ministry of University and Research, within a framework agreement between Lombardy Region and National Research Council of Italy (No. 17125, 27/09/2012).

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Conflict of Interest Statement: The authors have no conflicts of interest to disclose in relation to the specific topic of the present manuscript.

The reviewer BD and handling editor declared their shared affiliation.

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19 Impact of co-morbid attention-deficit and hyperactivity disorder on cognitive function in male children with tourette syndrome: a controlled study

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Abstract

Objective Neuropsychological studies have highlighted the presence of specific cognitive deficits in two neurodevelopmental disorders affecting more commonly male children and often presenting in co-morbidity, Tourette syndrome (TS) and attention-deficit and hyperactivity disorder (ADHD). It is estimated that over 60% of children with TS present with co-morbid ADHD and the assessment of the relative contribution of tic symptoms and ADHD symptoms to cognitive problems in this patient population poses considerable challenges. We set out to determine the impact of co-morbid ADHD on cognitive function in male children with TS by conducting a controlled study with a comprehensive battery of neuropsychological tests.

Method Participants included four groups of unmedicated age- and gender-matched children (mean age 10–12 years, range 6–15 years; 85%–100% male gender): TS group (n=13 children with a diagnosis of uncomplicated or 'pure' TS), TS+ADHD group n=8 children with TS and co-morbid ADHD), ADHD group (39 children with ADHD in the absence of tics) and controls n=66 healthy children). All patients had a DSM-validated diagnosis and were recruited from the Child Neuropsychiatry Unit, Varese, Italy, whereas healthy controls were randomly selected from a pool of research volunteers from local schools. Following clinical assessment, each participant completed a standardised battery of neuropsychological tests: the Wechsler Intelligence Scale for Children-III (Block Design test, Vocabulary test), Italian Battery for ADHD (Walk-Don't Walk test, Sustained Auditory Attention test, Stroop test, Sentence Completion test, Matching Familiar Figures test, Sustained Visual Attention test), Tower of London test, Corsi test, and Digit Span test.

Results All patient groups reported significantly lower scores than healthy controls across the neuropsychological tests involving executive functions. A specific pattern in cognitive performances emerged, showing that the TS+ADHD group was the most severely affected, followed by the ADHD group and the TS group. This was particularly evident from the results of the tests assessing planning ability (Block Design test, Matching Familiar Figures test, Tower of London test), inhibitory function (Walk-Don't Walk test, Stroop test, Matching Familiar Figures test), working memory (Sustained Auditory Attention test, Corsi test, Digit Span test) and visual attention (Walk-Don't Walk test, Matching Familiar Figures test, Sustained Visual Attention test), but not auditory attention (Sustained Auditory Attention test).

Conclusion Although problems in executive functions are more common in all patient groups than healthy controls, deficits in planning ability, inhibitory function, working memory and visual attention reported by children with TS appear to be more strongly related to the presence of co-morbid ADHD symptoms.

The multiple phenotypes of Tourette syndrome and attention-deficit hyperactivity disorder

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To the editors

We read with interest the recent Letter to the Editor by Mao and Yang (Mao and Yang, 2017) and we are pleased that our study on the impact of co-morbid attention deficit hyperactivity disorder (ADHD) on cognitive function in male children with Tourette syndrome (TS) (Termine et al., 2016) elicited praise and comments. In summary, our participants included four matched groups of 6- to 15-year-old male children who were not taking medications: TS (n=13), TS+ADHD (n=8), ADHD (n=39), healthy controls (n=66). All participants underwent a standardised psychometric battery of neuropsychological tests, in addition to clinical assessment. We found that problems in executive functions were more common in patients with neurodevelopmental disorders (TS and/or ADHD) than healthy controls. Moreover, the TS+ADHD group was the most severely affected, followed by the ADHD group and the TS group, particularly in the neuropsychological tests tapping into planning ability, inhibitory function, working memory, and visual attention. Overall, our preliminary findings suggested that a specific set of executive function deficits could be more strongly related to the presence of co-morbid ADHD symptoms than core TS symptoms.

The problem of the relative contribution of tic symptoms and ADHD symptoms to cognitive deficits in patients with TS is an under-investigated research area posing considerable challenges, which were only partially addressed by our controlled study paradigm. Specifically, we agree with the points raised by Mao and Yang (Mao and Yang, 2017) that further research is needed to confirm our preliminary findings and to better disentangle the relative contributions of tics and ADHD symptoms to cognitive function in male children with uncomplicated TS and TS+ADHD, in comparison to children with ADHD and healthy controls. Of particular interest is the observation that both TS and ADHD are heterogeneous neurodevelopmental conditions characterised by a spectrum of clinical presentations or discrete phenotypes (Bernfeld, 2012; Martino et al., 2013). Although it has not been established whether there is a definite link between one particular ADHD subtype and specific cognitive deficits, it is likely that future studies with more in-depth characterization of the clinical samples will add key contributions to our understanding of the cognitive

profiles of TS+ADHD populations, as well as their underlying neurobiological correlates (Mao and Yang, 2017). For example, the findings of a recent study suggested that executive function patterns are different in children with different ADHD subtypes, as the combined ADHD subtype appears to be associated with more significant problems in the perseveration and response inhibition domains (Ahmadi et al., 2014). Current evidence shows that the existence of multiple phenotypes is an important aspect of TS research, as chronic tic disorders have increasingly been re-conceptualized as clinically heterogeneous disorders spanning a motor-behavioural-cognitive continuum. Different clinical phenotypes have been shown to preferentially affect different aspects of health-related quality of life (Eddy et al., 2012) and there is the possibility that impulsivity as a feature of specific subtypes of both TS and ADHD predicts the presence of selective neuropsychological deficits (Frank et al., 2011). Likewise, the standardized characterization of ADHD symptom severity, as well as tic severity, is likely to provide one of the missing pieces of the multifaceted jig-saw of neurocognitive function in young patients affected by both conditions.

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(Delibera n. 406 - 2014 del 04/06/2014 Progetti NPI)
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