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## **BIBLIOGRAFIA ADHD AGOSTO 2016**

Acta Neuropsychiatr. 2016;28:5.

### **ADHD.**

#### ***Rataemane S.***

Attention deficit/hyperactivity disorder (ADHD) is characterized by symptoms of inattention and/or hyperactivity/impulsivity. The disorder is increasingly understood to be highly prevalent (up to 5% or more of children and 2% of adults) {Polanczyk, 2014} and associated with significant morbidity and functional impairment {Association, 2013}. Furthermore, the neurobiological basis and appropriate management of the disorder are becoming increasingly better understood {Sharma, A., et.al 2014}. Nevertheless, ADHD and its pharmacological management has frequently been the subject of negative media attention {Efron, 2015}. It has been claimed that in some schools, there is over-diagnosis of the disorder and that medication is simply used to control behaviour in healthy children. Concerns have been raised about the potential for abuse of methylphenidate and claims have been made about serious adverse events. While over-diagnosis in some settings may occur, a far more likely occurrence is under-diagnosis. Given the high prevalence of ADHD, the number of scripts written for methylphenidate in South Africa presumably reflects under-treatment. And given the serious consequences of untreated ADHD such as increase in subsequent antisocial personality traits and substance abuse {Shaw, M, et.al 2012}, such under-treatment is in fact an important concern. Co-morbidities such as conduct disorders, substance abuse, poor educational performance and underlying physical disorders need serious attention.

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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. 2016;1-9.

**RETROSPECTIVE ASSESSMENT OF CHILDHOOD ADHD SYMPTOMS FOR DIAGNOSIS IN ADULTS: VALIDITY OF A SHORT 8-ITEM VERSION OF THE WENDER-UTAH RATING SCALE.**

**Das D, Vélez JI, Acosta MT, et al.**

The Wender-Utah Rating Scale (WURS) is a widely used self-report instrument for retrospective assessment of childhood ADHD. However, many WURS items are not specific to ADHD. Here, we investigated the effect of excluding these items on the performance of the WURS in predicting adult ADHD based on previous diagnosis and current clinically significant symptoms. The study was conducted on a sample of adults (n = 1014; 48 % male) participating in a family-based investigation of ADHD. Participants completed the 61-item WURS questionnaire and the 66-item Conners Adult ADHD Rating Scale. Receiver operating characteristic (ROC) curves were used to compare the performance of the eight-item WURS (WURS-8) and the longer WURS-25 in predicting previous ADHD diagnosis and current clinically significant ADHD symptoms. WURS-8 and WURS-25 have approximately the same power to predict adult ADHD, based on either previous diagnosis or current symptoms (area under the ROC curves >0.8). WURS-8 performs at least as well as the longer WURS-25 in predicting adult ADHD. This 8-item questionnaire is thus a valid instrument and is especially useful for screening for ADHD in large epidemiological samples.

ADHD Atten Deficit Hyperact Disord. 2016;1-8.

**IS EMOTION RECOGNITION THE ONLY PROBLEM IN ADHD? EFFECTS OF PHARMACOTHERAPY ON FACE AND EMOTION RECOGNITION IN CHILDREN WITH ADHD.**

**Demirci E, Erdogan A.**

The objectives of this study were to evaluate both face and emotion recognition, to detect differences among attention deficit and hyperactivity disorder (ADHD) subgroups, to identify effects of the gender and to assess the effects of methylphenidate and atomoxetine treatment on both face and emotion recognition in patients with ADHD. The study sample consisted of 41 male, 29 female patients, 8–15 years of age, who were diagnosed as having combined type ADHD (N = 26), hyperactive/impulsive type ADHD (N = 21) or inattentive type ADHD (N = 23) but had not previously used any medication for ADHD and 35 male, 25 female healthy individuals. Long-acting methylphenidate (OROS-MPH) was prescribed to 38 patients, whereas atomoxetine was prescribed to 32 patients. The reading the mind in the eyes test (RMET) and Benton face recognition test (BFRT) were applied to all participants before and after treatment. The patients with ADHD had a significantly lower number of correct answers in child and adolescent RMET and in BFRT than the healthy controls. Among the ADHD subtypes, the hyperactive/impulsive subtype had a lower number of correct answers in the RMET than the inattentive subtypes, and the hyperactive/impulsive subtype had a lower number of correct answers in short and long form of BFRT than the combined and inattentive subtypes. Male and female patients with ADHD did not differ significantly with respect to the number of correct answers on the RMET and BFRT. The patients showed significant improvement in RMET and BFRT after treatment with OROS-MPH or atomoxetine. Patients with ADHD have difficulties in face recognition as well as emotion recognition. Both OROS-MPH and atomoxetine affect emotion recognition. However, further studies on the face and emotion recognition are needed in ADHD.

ADHD Atten Deficit Hyperact Disord. 2016;1-8.

**THE ROLE OF SLEEP QUALITY AND QUANTITY IN MODERATING THE EFFECTIVENESS OF MEDICATION IN THE TREATMENT OF CHILDREN WITH ADHD.**

**Morash-Conway J, Gendron M, Corkum P.**

The current study examined: (1) whether long-acting stimulant medication is effective in improving performance on measures of memory, attention, and academic productivity; and (2) whether sleep impacts the relationship between medication and performance. Participants were 21 newly diagnosed, medication-naïve children (mean age = 9.1 years) with ADHD, who participated in a 4-week blinded placebo-controlled randomized trial of long-acting MPH. Participants underwent assessments of sleep (i.e., polysomnography)

and of cognitive performance. Long-acting stimulant medication was found to be an effective treatment for enhancing alerting attention, executive attention, working memory, and academic productivity, but resulted in poorer sleep. Moreover, sleep duration was found to impact the treatment response to medication, in that longer sleep duration at baseline was related to improved executive attention. These results underscore the importance of evaluating and monitoring sleep when prescribing stimulant medication as a treatment for ADHD in children.

Am J Psychiatry. 2016 Jan;173:34-43.

**ASSOCIATION BETWEEN ADHD AND OBESITY: A SYSTEMATIC REVIEW AND META-ANALYSIS.**

**Cortese S, Moreira-Maia CR, St FD, et al.**

**OBJECTIVE:** Impulsivity and inattention related to attention deficit hyperactivity disorder (ADHD) may increase food intake and, consequently, weight gain. However, findings on the association between obesity/overweight and ADHD are mixed. The authors conducted a meta-analysis to estimate this association.

**METHOD:** A broad range of databases was searched through Aug. 31, 2014. Unpublished studies were also obtained. Study quality was rated with the Newcastle-Ottawa Scale. Random-effects models were used.

**RESULTS:** Forty-two studies that included a total of 728,136 individuals (48,161 ADHD subjects; 679,975 comparison subjects) were retained. A significant association between obesity and ADHD was found for both children (odds ratio=1.20, 95% CI=1.05-1.37) and adults (odds ratio=1.55, 95% CI=1.32-1.81). The pooled prevalence of obesity was increased by about 70% in adults with ADHD (28.2%, 95% CI=22.8-34.4) compared with those without ADHD (16.4%, 95% CI=13.4-19.9), and by about 40% in children with ADHD (10.3%, 95% CI=7.9-13.3) compared with those without ADHD (7.4%, 95% CI=5.4-10.1). The significant association between ADHD and obesity remained when limited to studies 1) reporting odds ratios adjusted for possible confounding factors; 2) diagnosing ADHD by direct interview; and 3) using directly measured height and weight. Gender, study setting, study country, and study quality did not moderate the association between obesity and ADHD. ADHD was also significantly associated with overweight. Individuals medicated for ADHD were not at higher risk of obesity.

**CONCLUSIONS:** This study provides meta-analytic evidence for a significant association between ADHD and obesity/overweight. Further research should address possible underlying mechanisms and the long-term effects of ADHD treatments on weight in individuals with both ADHD and obesity.

Aust New Zealand J Psychiatry. 2016;50:114-15.

**COMPARING THE TIME-COURSE OF EFFICACY OF LISDEXAMFETAMINE DIMESYLATE AND OSMOTIC CONTROLLED-RELEASE METHYLPHENIDATE IN CHILDREN AND ADOLESCENTS WITH ADHD.**

**Coghill D, Nagy P, Frick G, et al.**

**Background:** Lisdexamfetamine dimesylate (LDX) and osmotic controlled-release methylphenidate (OROS-MPH) are stimulant treatments for attention deficit hyperactivity disorder (ADHD).

**Objectives:** To compare the time-course of the efficacy of LDX and OROS-MPH in children and/or adolescents with ADHD in three short-term (6-8 weeks), randomized, controlled trials.

**Methods:** In the studies SPD489-405 (flexible-dose) and SPD489-406 (fixed-dose), the efficacy of LDX (30-70 mg) and OROS-MPH (18-72 mg) was compared head-to-head in adolescents (13-17 years). The study SPD489-325 (flexible-dose) included children and adolescents (6-17 years) and LDX (30-70 mg) and OROS-MPH (18-54 mg) were compared post hoc. Participants were randomized 2:2:1 to LDX, OROS-MPH and placebo in SPD489-405/406 and 1:1:1 in SPD489-325. ADHD Rating Scale IV (ADHD-RS-IV) total scores were assessed at each study visit.

**Findings:** The differences (LDX - OROS-MPH) in a least-squares mean (95% confidence interval) changed from baseline: ADHD-RS-IV total scores were statistically significant at week 1 in all three studies (SPD489-405, -2.6 [-4.5, -0.8],  $p = 0.0047$ ; SPD489-406, -2.0 [-3.8, -0.3],  $p = 0.0242$ ; SPD489-325, -3.3 [-5.9, -0.6],  $p = 0.016$ ), at week 6 in SPD489-406 (-3.4 [-5.4, -1.3],  $p = 0.0013$ ) and at endpoint in SPD489-325 (-5.6 [-8.4,

-2.7],  $p < 0.001$ ), but not at week 8 in SPD489-405 (-2.1 [-4.3, 0.2],  $p = 0.0717$ ). Safety profiles were consistent with those from previous studies.

**Conclusions:** LDX was associated with greater improvements in ADHD symptoms than OROS-MPH at week 1 in all three studies, at week 6 in SPD489-406 and at endpoint in SPD489-325, but not at week 8 in SPD489-405.

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Aust New Zealand J Psychiatry. 2016;50:94.

**HISTORY, PREVALENCE AND DIAGNOSIS OF ATTENTION DEFICIT HYPERACTIVITY DISORDER.**

**Perera M.**

**Background:** Attention deficit hyperactivity disorder (ADHD) is a neurodevelopmental disorder. Its symptoms were first described many centuries ago. The estimates of its prevalence vary between 5% and 10% of children in a general population and half of that in the adult. The diagnosis can be made for the first time in the adult. The condition may be co-morbid with other diagnoses.

**Objectives:** Demonstrate historical aspects, explore epidemiology of ADHD and discuss diagnosis in an adult and the different problems that are present when the child with ADHD transitions to an adult with ADHD.

**Methods:** A careful history is the cornerstone of diagnosis, with particular relevance to behavioural problems beginning in childhood. Collateral information and corroboration are required. A family history of similar behaviours is sought. Symptom checklists that are of assistance will be made known. Inquiry needs to be made regarding co-morbid conditions. If ADHD is diagnosed in childhood, the relevant documentation and review of the current problems are required.

**Findings:** Making a de novo diagnosis of ADHD in the adult requires careful screening and evaluation. Drug seekers for hedonistic purposes need to be eliminated. The needs of the child transitioning to adult may have changed. Co-morbid conditions will be identified.

**Conclusions:** ADHD persists into adulthood. Some people with ADHD are diagnosed only later in life. Care needs to be exercised in diagnosing the condition for the first time in an adult. Other medical and psychological problems need to be identified.

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Aust New Zealand J Psychiatry. 2016;50:164.

**HISTORICAL DESCRIPTIONS OF ATTENTION DEFICIT HYPERACTIVITY DISORDER.**

**Perera D.**

**Background:** Some argue that attention deficit hyperactivity disorder (ADHD) is a result of the adverse conditions of modern society and questioning it as a nosological entity. However, it appears that there are many early descriptions akin to the present-day condition.

**Objectives:** To determine whether the early writings described what we know today as ADHD.

**Methods:** A search of the literature using PubMed with key words 'History' and 'ADHD' and equivalent terms did not yield relevant articles. Hence, a strategic search was performed using cross-references as well as searching on PubMed for a known article and then obtaining related articles.

**Findings:** The available literature suggests the existence of this disorder dating back to the 18th century with the earliest reference to it made in the late 1700's (Bader and Hadjikhani, 2013). Fidgety Philip and Johnny Look in the Air are from a 19th century children's story book depicting ADHD-type behaviour (Thome and Jacobs, 2004). Minimal brain dysfunction and hyperkinetic disease of infancy, also known as Kramer - Pollnow syndrome, were all terms describing ADHD symptomology in children (Lange et al., 2010). The terminology for the syndrome has evolved and continues to be classified in the current Diagnostic and Statistical Manual of Mental Disorders, Fifth edition (DSM- 5) as well as the International Classification of Diseases (ICD)-10-CM.

**Conclusions:** Children presenting with symptoms of inattention, hyperactivity and impulsivity have been described by several authors during the last 200 years. These descriptions are consistent with the modern diagnostic criteria for ADHD. It is a condition that has an ancient history.

Aust New Zealand J Psychiatry. 2016;50:30.

**DEFAULT NETWORK, ATTENTION DEFICIT HYPERACTIVITY DISORDER AND EMOTIONAL REGULATION.**

**Levy F, Silberstein RB, Pipingas A, et al.**

**Background:** It has been suggested that the inattentiveness in attention deficit hyperactivity disorder (ADHD) is due to inadequate suppression of the default mode network (DMN), and increased activity is associated with intrusion of self-referential thoughts. A number of authors have postulated that ADHD represents a deficit in inhibition of DMN activity, but few have researched relationships with emotional regulation. The literature on the DMN and ADHD is briefly reviewed. A recent brain mapping study by Silberstein et al. utilizing a continuous performance task (CPT) A-X task that showed differences in children with ADHD in the A-X interval is cited with possible implications for emotional regulation.

**Objectives:** To briefly review studies of ADHD and DMN and to report on functional connectivity during an A-X CPT in a sample of 42 males with ADHD and 25 controls.

**Methods:** The technique of steady-state evoked potential (SSVEP) during the A-X CPT was utilized and event-related partial coherence was compared to a reference task across 2016 electrode pairs.

**Findings:** The control group exhibited high levels of default mode network activity during a low-demand reference task, which was suppressed during the A-X task, while the group with ADHD exhibited low levels of default mode network activity during this task.

**Conclusions:** The sentinel and inhibition hypotheses of DMN and ADHD are compared in relation to emotional regulation and task performance.

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Aust New Zealand J Psychiatry. 2016;50:30.

**INTEGRITY OF AMYGDALA SUBREGION-BASED FUNCTIONAL NETWORKS AND EMOTIONAL LABILITY IN DRUG-NAIVE BOYS WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER.**

**Yu XY, Liu L, Chen W, et al.**

**Background:** Attention deficit hyperactivity disorder (ADHD) is frequently associated with deficits in emotional self-regulation. With the amygdala being a key brain region involved in emotional regulation, recent studies demonstrated alterations of amygdala networks related to emotional lability (EL) of children with ADHD. However, the amygdala is a functionally heterogeneous structure, comprising distinct main subregions: the basolateral (BLA), centromedial (CMA) and superficial (SFA).

**Objectives:** This study evaluated the integrity of amygdala subregion-based functional networks in boys with ADHD and their association with EL symptoms.

**Methods:** This study examined resting-state functional connectivity (RSFC) of amygdala subregions using resting-state functional magnetic resonance imaging in 35 drug-naive boys with ADHD and 30 age-matched healthy boys. We also explored the relationships between the altered RSFC of amygdala subregions and EL scores in ADHD.

**Findings:** Widespread reduced RSFC patterns were detected between amygdala subregions and the dorsal frontoparietal cortices, temporal cortex and limbic regions in boys with ADHD. More specifically, the BLA networks were altered in RSFC with thalamus and vermis; altered RSFC of the CMA was found with the superior temporal gyrus/pole and insula, precuneus and cerebellum; and the RSFC between the SFA and the dorsal frontoparietal cortices was reduced. Among the group with ADHD, high EL scores were associated with reduced negative RSFC between the SFA and the dorsolateral prefrontal cortex, as well as the inferior parietal lobe.

**Conclusions:** Our findings provide preliminary evidence for diffuse alterations of amygdala subregion-based networks being associated with ADHD. Within ADHD, EL scores were associated with weaker SFA-frontoparietal networks which are involved in the hypothesized topdown ('effortful') regulation of emotion.

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Aust New Zealand J Psychiatry. 2016;50:162.

**LONG-TERM SAFETY AND EFFICACY OF LISDEXAMFETAMINE DIMESYLATE BY AGE SUBGROUP IN CHILDREN AND ADOLESCENTS WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER.**

**Coghill D, Hern+índez Otero I, Nagy P, et al.**

**Background:** Attention deficit hyperactivity disorder (ADHD) requires long-term management.

**Objectives:** To evaluate the long-term safety and efficacy of lisdexamfetamine dimesylate (LDX) in children and adolescents with ADHD in a 2-year, open-label study.

**Methods:** Children (6-12 years) or adolescents (13- 17 years) with ADHD received once-daily, dose-optimized LDX (30, 50 or 70 mg) for 104 weeks. Safety monitoring included treatment-emergent adverse events (TEAEs) and vital signs. Efficacy was assessed as a secondary outcome.

**Findings:** Of the 314 participants enrolled, 191 completed the study. In the safety population (n = 314), TEAEs were reported by 89.8% of participants, led to discontinuation in 12.4% and were reported as serious by 8.9%. TEAEs reported by 10.0% of participants were decreased appetite, nasopharyngitis, headache, decreased weight, insomnia, initial insomnia, irritability and pyrexia. The mean (standard deviation) increases from baseline to last on-treatment assessment (LOTA) in vital signs were systolic blood pressure, 3.4 (10.33) mmHg; diastolic blood pressure, 3.2 (9.05) mmHg; pulse, 7.0 (11.60) bpm. When categorized by age, TEAEs were reported by 181 of 202 (89.6%) children and 101 of 112 (90.2%) adolescents. The mean (95% confidence interval) change from baseline to LOTA in ADHD-Rating-Scale-IV total score was -25.8 (-27.0, -24.5) in the full analysis set (n = 299), -26.3 (-27.9, -24.6) in children (n = 189) and -24.9 (-26.9, -23.0) in adolescents (n = 110); all ps < 0.001.

**Conclusions:** The safety profile of LDX in children and adolescents in this long-term study was similar to that reported in previous short-term and long-term studies. The efficacy of LDX was demonstrated throughout the 2-year study.

Aust New Zealand J Psychiatry. 2016;50:28-29.

**EMOTIONAL LABILITY (EL) AMONG CHILDREN WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER IN AUSTRALASIA: FACTORIAL VALIDITY, NEURAL CIRCUITRY CORRELATES AND COMPASSIONATE MIND TRAINING.**

**Chen W, Liu L, Yu XY, et al.**

**Background:** Emotional lability (EL) and oppositional defiance disorder (ODD) frequently co-occur with attention deficit hyperactivity disorder (ADHD). Their relationships and neurobiological underpinnings are still poorly understood. This symposium focuses on the recent research and findings on EL and ADHD in an Australasian research network, spanning Western Australia, New South Wales, Beijing and Hong Kong.

**Objectives:** This symposium explores the following: The factorial validity of EL as a construct distinct and independent from ODD;The neural correlates of EL in relation to resting state connectivity of amygdalal subregions with other brain regions;The potential roles of default mode network regarding EL;The applicability of compassion mind therapy as a treatment option for children with high levels of self-criticism, shame and emotional dysregulation.

**Methods:** A diverse range of methods were used to investigate these objectives.

**Findings:** The first presentation demonstrates that EL is distinct from 'mood/affect' and other subdimensions of ODD by both exploratory and confirmatory analyses. The second presentation reports the deficits in connectivity between top-down networks and amygdalar subregions detected in ADHD probands with higher levels of EL. The third presentation evaluates the relevance of the default mode network in emotional regulation. The fourth presentation examines the positive treatment effects of compassion mind therapy in a pilot study of children in Hong Kong.

**Conclusions:** EL is a clinically important presentation among children with ADHD, despite not being captured by the current major taxonomic systems. Studies reported in this symposium advance knowledge on EL with their scientific and clinical implications explored.

BMC Psychiatry. 2016;16.

**LINEAR AND NON-LINEAR ANALYSES OF CONNER'S CONTINUOUS PERFORMANCE TEST-II DISCRIMINATE ADULT PATIENTS WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER FROM PATIENTS WITH MOOD AND ANXIETY DISORDERS. Fasmer OB, Mjeldheim K, Førland W, et al.**

**Background:** Attention Deficit Hyperactivity Disorder (ADHD) is a heterogeneous disorder. Therefore it is important to look for factors that can contribute to better diagnosis and classification of these patients. The aims of the study were to characterize adult psychiatric out-patients with a mixture of mood, anxiety and attentional problems using an objective neuropsychological test of attention combined with an assessment of mood instability.

**Method:** Newly referred patients (n = 99; aged 18-65 years) requiring diagnostic evaluation of ADHD, mood or anxiety disorders were recruited, and were given a comprehensive diagnostic evaluation including the self-report form of the cyclothymic temperament scale and Conner's Continuous Performance Test II (CPT-II). In addition to the traditional measures from this test we have extracted raw data and analysed time series using linear and non-linear mathematical methods.

**Results:** Fifty patients fulfilled criteria for ADHD, while 49 did not, and were given other psychiatric diagnoses (clinical controls). When compared to the clinical controls the ADHD patients had more omission and commission errors, and higher reaction time variability. Analyses of response times showed higher values for skewness in the ADHD patients, and lower values for sample entropy and symbolic dynamics. Among the ADHD patients 59 % fulfilled criteria for a cyclothymic temperament, and this group had higher reaction time variability and lower scores on complexity than the group without this temperament.

**Conclusion:** The CPT-II is a useful instrument in the assessment of ADHD in adult patients. Additional information from this test was obtained by analyzing response times using linear and non-linear methods, and this showed that ADHD patients with a cyclothymic temperament were different from those without this temperament.

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BMC Psychiatry. 2016;16:11.

**IS ADJUNCTIVE PHARMACOTHERAPY IN ATTENTION-DEFICIT/HYPERACTIVITY DISORDER COST-EFFECTIVE IN CANADA: A COST-EFFECTIVENESS ASSESSMENT OF GUANFACINE EXTENDED-RELEASE AS AN ADJUNCTIVE THERAPY TO A LONG-ACTING STIMULANT FOR THE TREATMENT OF ADHD.**

**Lachaine J, Sikirica V, Mathurin K.**

**BACKGROUND:** Attention-deficit/hyperactivity disorder (ADHD) is a common psychiatric disorder in children, with worldwide prevalence of ADHD varying from 5.9 to 7.1 %, depending on the reporter. In case of inadequate response to stimulants, combination therapy of stimulants and an adjunctive medication may improve the control of ADHD symptoms, reduce the dose-limiting adverse events, and help control comorbidities. To date, the only medication to be used for adjunctive therapy to psychostimulants is guanfacine extended release (GXR). The aim of this study was to assess the economic impact of GXR as an adjunct therapy with long-acting stimulants (GXR + stimulant) compared to long-acting stimulant monotherapy (stimulant alone) in the treatment of children and adolescents with ADHD in Canada.

**METHOD:** A Markov model was developed using health states defined based on the clinician-reported Clinical Global Impression-Severity (CGI-S) score (normal, mild, moderate, severe). Transition probabilities were calculated based on patient-level data from a published study. Long-acting stimulants available in Canada were considered in the base-case model: amphetamine mixed salts, methylphenidate HCl formulations, and lisdexamfetamine dimesylate. Analyses were conducted from a Canadian Ministry of Health (MoH; Ontario) and a societal perspective over a 1-year time horizon with weekly cycles.

**RESULTS:** Over a 1-year time horizon, GXR + stimulant was associated with 0.655 quality-adjusted life year (QALY), compared to 0.627 QALY with stimulant alone, for a gain of 0.028 QALY. From a MoH perspective, GXR+ stimulant and stimulant alone were associated with total costs of \$CA1,617 and \$CA949, respectively (difference of \$CA668), which resulted in an incremental cost-effectiveness ratio (ICER) of \$CA23,720/QALY. From a societal perspective, GXR + stimulant and stimulant alone were associated with total costs of \$CA3,915 and \$CA3,582, respectively (difference of \$CA334), which resulted in an ICER of \$CA11,845/QALY. Probabilistic sensitivity analysis (PSA) of GXR + stimulant showed that it remains a cost-



effective strategy in 100 % of the simulations from both perspectives in numerous PSA and one-way sensitivity analyses, relative to a willingness to pay threshold of \$50,000/QALY.

**CONCLUSIONS:** This economic evaluation demonstrates that GXR + stimulant is cost-effective compared to stimulant alone in the treatment of children and adolescents with ADHD in Canada

Br J Nutr. 2016 Jan;115:361-73.

**A RANDOMISED DOUBLE-BLIND PLACEBO-CONTROLLED TRIAL INVESTIGATING THE BEHAVIOURAL EFFECTS OF VITAMIN, MINERAL AND N-3 FATTY ACID SUPPLEMENTATION IN TYPICALLY DEVELOPING ADOLESCENT SCHOOLCHILDREN.**

**Tammam JD, Steinsaltz D, Bester DW, et al.**

Nutrient deficiencies have been implicated in anti-social behaviour in schoolchildren; hence, correcting them may improve sociability. We therefore tested the effects of vitamin, mineral and n-3 supplementation on behaviour in a 12-week double-blind randomised placebo-controlled trial in typically developing UK adolescents aged 13-16 years (n 196). Changes in erythrocyte n-3 and 6 fatty acids and some mineral and vitamin levels were measured and compared with behavioural changes, using Conners' teacher ratings and school disciplinary records. At baseline, the children's PUFA (n-3 and n-6), vitamin and mineral levels were low, but they improved significantly in the group treated with n-3, vitamins and minerals (P=0.0005). On the Conners disruptive behaviour scale, the group given the active supplements improved, whereas the placebo group worsened (F=5.555, d=0.35; P=0.02). The general level of disciplinary infringements was low, thus making it difficult to obtain improvements. However, throughout the school term school disciplinary infringements increased significantly (by 25 %; Bayes factor=115) in both the treated and untreated groups. However, when the subjects were split into high and low baseline infringements, the low subset increased their offences, whereas the high-misbehaviour subset appeared to improve after treatment. But it was not possible to determine whether this was merely a statistical artifact. Thus, when assessed using the validated and standardised Conners teacher tests (but less clearly when using school discipline records in a school where misbehaviour was infrequent), supplementary nutrition might have a protective effect against worsening behavior.

Brain. 2016;139:2307-21.

**NEURAL, ELECTROPHYSIOLOGICAL AND ANATOMICAL BASIS OF BRAIN-NETWORK VARIABILITY AND ITS CHARACTERISTIC CHANGES IN MENTAL DISORDERS.**

**Zhang J, Cheng W, Liu Z, et al.**

Functional brain networks demonstrate significant temporal variability and dynamic reconfiguration even in the resting state. Currently, most studies investigate temporal variability of brain networks at the scale of single (micro) or whole-brain (macro) connectivity. However, the mechanism underlying time-varying properties remains unclear, as the coupling between brain network variability and neural activity is not readily apparent when analysed at either micro or macroscales. We propose an intermediate (meso) scale analysis and characterize temporal variability of the functional architecture associated with a particular region. This yields a topography of variability that reflects the whole-brain and, most importantly, creates an analytical framework to establish the fundamental relationship between variability of regional functional architecture and its neural activity or structural connectivity. We find that temporal variability reflects the dynamical reconfiguration of a brain region into distinct functional modules at different times and may be indicative of brain flexibility and adaptability. Primary and unimodal sensory-motor cortices demonstrate low temporal variability, while transmodal areas, including heteromodal association areas and limbic system, demonstrate the high variability. In particular, regions with highest variability such as hippocampus/parahippocampus, inferior and middle temporal gyrus, olfactory gyrus and caudate are all related to learning, suggesting that the temporal variability may indicate the level of brain adaptability. With simultaneously recorded electroencephalography/functional magnetic resonance imaging and functional magnetic resonance imaging/diffusion tensor imaging data, we also find that variability of regional functional architecture is

modulated by local blood oxygen level-dependent activity and  $\beta$ -band oscillation, and is governed by the ratio of intra- to inter-community structural connectivity. Application of the mesoscale variability measure to multicentre datasets of three mental disorders and matched controls involving 1180 subjects reveals that those regions demonstrating extreme, i.e. highest/lowest variability in controls are most liable to change in mental disorders. Specifically, we draw attention to the identification of diametrically opposing patterns of variability changes between schizophrenia and attention deficit hyperactivity disorder/autism. Regions of the default-mode network demonstrate lower variability in patients with schizophrenia, but high variability in patients with autism/attention deficit hyperactivity disorder, compared with respective controls. In contrast, subcortical regions, especially the thalamus, show higher variability in schizophrenia patients, but lower variability in patients with attention deficit hyperactivity disorder. The changes in variability of these regions are also closely related to symptom scores. Our work provides insights into the dynamic organization of the resting brain and how it changes in brain disorders. The nodal variability measure may also be potentially useful as a predictor for learning and neural rehabilitation.

Br J Clin Pharmacol. 2016;858-68.

**PRESCRIBING TRENDS OF ATTENTION-DEFICIT HYPERACTIVITY DISORDER (ADHD) MEDICATIONS IN UK PRIMARY CARE, 1995–2015.**

**Renoux C, Shin JY, Dell'Aniello S, et al.**

**Aim:** The aim of the present study was to describe the prescription of medications for attention-deficit hyperactivity disorder (ADHD) in the UK between 1995 and 2015.

**Methods:** Using the Clinical Practice Research Datalink (CPRD), we defined a cohort of all patients aged 6–45 years, registered with a general practitioner between January 1995 and September 2015. All prescriptions of methylphenidate, dexamphetamine/lisdexamphetamine and atomoxetine were identified and annual prescription rates of ADHD were estimated using Poisson regression.

**Results:** Within a cohort of 7 432 735 patients, we identified 698 148 prescriptions of ADHD medications during 41 171 528 person-years of follow-up. Usage was relatively low until 2000, during which the prescription rate was 42.7 [95% confidence interval (CI) 20.9, 87.2] prescriptions per 10 000 persons, increasing to 394.4 (95% CI 296.7, 524.2) in 2015, corresponding to an almost 800% increase (rate ratio 8.87; 95% CI 7.10, 11.09). The increase was seen in all age groups and in both sexes but was steepest in boys aged 10–14 years. The prescription rate in males was almost five times that of females. Methylphenidate remained the most prescribed drug during the 20-year study period, representing 88.9% of all prescriptions in the 6–24 year old group, and 63.5% of all prescriptions in adults (25–45 years of age).

**Conclusions:** Prescription rates of ADHD medications have increased dramatically in the past two decades. This may be due, at least in part, to both an increase in the number of patients diagnosed with ADHD over time and a higher percentage of those patients treated with medication.

Child Adolesc Psychiatry Ment Health. 2016;10.

**REDUCED PAIN PERCEPTION IN CHILDREN AND ADOLESCENTS WITH ADHD IS NORMALIZED BY METHYLPHENIDATE.**

**Wolff N, Rubia K, Knopf H, et al.**

**Background:** The present study examined pain perception in children and adolescents with ADHD and the interaction between pain perception and the administration of methylphenidate (MPH) in order to generate hypotheses for further research that will help to clarify the association between ADHD diagnosis, MPH treatment and pain perception.

**Methods:** We included 260 children and adolescents of the "German Health Interview and Examination Survey for Children and Adolescents" (KiGGS) and analyzed parent's assessments of children's pain distribution and pain perception, as well as the influence of MPH administration on pain perception in affected children and adolescents.

**Results:** Pain perception was associated with ADHD and MPH administration, indicating that children and adolescents suffering from ADHD without MPH treatment were reported to have lower pain perception compared to both, healthy controls (HC) and ADHD patients medicated with MPH.

**Conclusion:** We suggest that reduced pain perception in children and adolescents with ADHD not medicated with MPH may lead to higher risk tolerance by misjudgments of dangerous situations, expanding the importance of MPH administration in affected children and adolescents.

Child Neuropsychol. 2016;22:420-42.

**RESPONSE INHIBITION DIFFICULTIES IN PRETERM CHILDREN AGED 9-12 YEARS: RELATIONS WITH EMOTION AND BEHAVIOR.**

**Reveillon M, Borradori TC, Monnier M, et al.**

Previous studies with children have demonstrated inhibition difficulties associated with prematurity, but the question of potentially catching up with a delay in inhibition processes before adolescence still remains. Moreover, preterm adolescents are more at risk than their term-born peers for presenting behavioral problems such as emotional difficulties and attention deficit/hyperactivity disorder. In addition to examining response inhibition, this study addressed, for the first time, the impact of an emotional context on response inhibition abilities and its relation to behavioral problems in late school-aged preterm children. Fifty-eight preterm children aged 9-12 years were compared with 61 controls on two versions of a stop-signal task, the Delay Frustration Task, and the Strengths and Difficulties Questionnaire. Results showed general difficulties in inhibiting a response, rather than a specific impact of emotional context in preterm children. Compared with controls, these children exhibited more and longer button presses in a delay situation, as well as faster go reaction times associated with lower probability of inhibition in the stop-signal tasks. These difficulties reflected impulsivity and were associated with higher hyperactivity/inattention and conduct problems. Additionally, intrauterine growth restriction was found to be an additional perinatal risk factor for hyperactivity/inattention symptoms. These findings suggest that remaining inhibition difficulties in the preterm population at preadolescence could reveal increasing behavioral issues.

Child Neuropsychol. 2016;22:345-65.

**EXECUTIVE AND ATTENTIONAL CONTRIBUTIONS TO THEORY OF MIND DEFICIT IN ATTENTION DEFICIT/HYPERACTIVITY DISORDER (ADHD).**

**Mary A, Slama H, Mousty P, et al.**

Attention deficit/hyperactivity disorder (ADHD) in children has been associated with attentional and executive problems, but also with socioemotional difficulties possibly associated with deficits in Theory of Mind (ToM). Socioemotional problems in ADHD are associated with more negative prognoses, notably interpersonal, educational problems, and an increased risk of developing other psychiatric disorders that emphasize the need to clarify the nature of their ToM deficits. In this study, we hypothesized that ToM dysfunction in children with ADHD is largely attributable to their attentional and/or executive deficits. Thirty-one children with ADHD (8-12 years, IQ > 85) and 31 typically developing (TD) children were assessed using executive functions (inhibition, planning, and flexibility) and attentional tasks, as well as two advanced ToM tasks (Reading the Mind in the Eyes and Faux Pas) involving different levels of executive control. Children with ADHD performed more poorly than TD children in attentional, executive function, and ToM tasks. Linear regression analyses conducted in the ADHD group indicated that inhibition scores predicted performance on the "Faux Pas" task the best, while attention scores were the best for predicting performance on the Reading the Mind in the Eyes task. When controlled for inhibition and attentional variables, ToM performance in children with ADHD was actually similar to TD children. Contrarily, controlling for ToM scores did not normalize performance for inhibition and attentional tasks in children with ADHD. This unidirectional relationship suggests that deficits in the EF and attentional domains are responsible for ToM deficits in ADHD, which therefore may contribute to their socioemotional difficulties.

Child Neuropsychol. 2016;22:870-88.

**EXECUTIVE FUNCTIONING PROFILES FROM THE BRIEF ACROSS PEDIATRIC MEDICAL DISORDERS: AGE AND DIAGNOSIS FACTORS.**

**Krivitzky LS, Walsh KS, Fisher EL, et al.**

The objective of the study was to compare executive functioning (EF) profiles across several pediatric medical conditions and explore the influence of age of diagnosis and evaluation. A retrospective, cross-sectional study of 734 children aged 5 to 18 years was conducted across five medical groups (brain tumor, leukemia [ALL], epilepsy [EPI], neurofibromatosis type 1 [NF1], and ornithine transcarbamylase deficiency [OTC-D]), attention deficit hyperactivity disorder (ADHD) controls, and matched healthy controls. We compared groups across the scales of a parent-completed Behavior Rating Inventory of Executive Functioning (BRIEF) using a repeated measures analysis of variance (ANOVA). Separate ANOVAs were conducted to look at age factors. The results showed that the ADHD group differed from all other groups and had the highest level of reported EF problems. The NF1 and OTC-D groups differed significantly from the healthy comparison group for overall EF problems, while the EPI and cancer groups did not. Working memory was the most elevated scale across medical groups, followed by plan/organize. Children with medical disorders were two to four times more likely than healthy controls to have clinically significant problems in several EF domains. There was a main effect for age at diagnosis and age at evaluation. A subset of children with medical disorders were found to have parent-reported EF difficulties, with particular vulnerability noted in working memory and organizational/planning skills. This has relevance for the development of interventions that may be helpful across disorders. Children with particular diagnoses and earlier age of diagnosis and evaluation had greater reported EF problems.

Child Neuropsychol. 2016;1-27.

**HETEROGENEITY IN ADHD: NEUROCOGNITIVE PREDICTORS OF PEER, FAMILY, AND ACADEMIC FUNCTIONING.**

**Kofler MJ, Sarver DE, Spiegel JA, et al.**

Childhood attention-deficit/hyperactivity disorder (ADHD) is associated with impairments in peer, family, and academic functioning. Although impairment is required for diagnosis, children with ADHD vary significantly in the areas in which they demonstrate clinically significant impairment. However, relatively little is known about the mechanisms and processes underlying these individual differences. The current study examined neurocognitive predictors of heterogeneity in peer, family, and academic functioning in a well-defined sample of 44 children with ADHD aged 8-13 years ( $M = 10.31$ ,  $SD = 1.42$ ; 31 boys, 13 girls; 81% Caucasian). Reliable change analysis indicated that 98% of the sample demonstrated objectively-defined impairment on at least one assessed outcome measure; 65% were impaired in two or all three areas of functioning. ADHD children with quantifiable deficits in academic success and family functioning performed worse on tests of working memory ( $d = 0.68$  to  $1.09$ ), whereas children with impaired parent-reported social functioning demonstrated slower processing speed ( $d = 0.53$ ). Dimensional analyses identified additional predictors of peer, family, and academic functioning. Working memory abilities were associated with individual differences in all three functional domains, processing speed predicted social functioning, and inhibitory control predicted family functioning. These results add to a growing literature implicating neurocognitive abilities not only in explaining behavioral differences between ADHD and non-ADHD groups, but also in the substantial heterogeneity in ecologically-valid functional outcomes associated with the disorder.

Child Psychiatry Hum Dev. 2016 Aug;47:574-82.

**DEMOGRAPHIC CHARACTERISTICS AND PSYCHIATRIC COMORBIDITY OF CHILDREN AND ADOLESCENTS DIAGNOSED WITH ADHD IN SPECIALIZED HEALTHCARE.**

**Joelsson P, Chudal R, Gyllenberg D, et al.**

Recent studies have shown an increasing incidence of attention-deficit/hyperactivity disorder (ADHD) among children diagnosed in specialized services. This study aims to describe children with ADHD in Finnish

specialized healthcare by reporting the demographic characteristics, time trends in diagnosis, psychiatric comorbidity, and the validity of register-based diagnoses. All the singletons born in Finland between 1991 and 2005 and diagnosed with ADHD by 2011 were identified and their psychiatric comorbidity data was obtained from the Finnish Hospital Discharge Register (FHDR). Parents of 69 patients were interviewed via telephone for a diagnostic validation. A total of 10,409 children were identified with ADHD, with a male:female ratio of 5.3:1 and a psychiatric comorbidity rate of 76.7 %. Of the validation sample 88 % met the diagnostic criteria of ADHD for DSM-IV. There is an increasing trend of ADHD diagnosis among both males and females. Psychiatric comorbidity is common and includes a wide range of disorders among children with ADHD. There was an increase of ADHD diagnoses especially among boys. More attention is needed to detect ADHD among girls in health services. Diagnoses in the FHDR show diagnostic validity and their sociodemographic patterns are in line with previous studies.

Child Psychiatry Hum Dev. 2016 Aug;47:618-26.

**THOUGHT DISORDER IN PRESCHOOL CHILDREN WITH ATTENTION DEFICIT/HYPERACTIVITY DISORDER (ADHD).**

**Hutchison AK, Kelsay K, Talmi A, et al.**

Preschool identification of and intervention for psychiatric symptoms has the potential for lifelong benefits. However, preschool identification of thought disorder, a symptom associated with long term risk for social and cognitive dysfunction, has received little attention with previous work limited to examining preschoolers with severe emotional and behavioral dysregulation. Using story-stem methodology, 12 children with ADHD and 12 children without ADHD, ages 4.0–6.0 years were evaluated for thought disorder. Thought disorder was reliably assessed (Cronbach's alpha = .958). Children with ADHD were significantly more likely than children without ADHD to exhibit thought disorder (75 vs 25 %; Fischer's Exact Test = .0391). Thought disorder can be reliably assessed in preschool children and is present in preschool children with psychiatric illness including preschool children with ADHD. Thought disorder may be identifiable in preschool years across a broad range of psychiatric illnesses and thus may be an appropriate target of intervention.

Child Psychiatry Hum Dev. 2016 Feb;47:35-42.

**PREVALENCE OF PSYCHIATRIC DISORDERS AMONG TURKISH CHILDREN: THE EFFECTS OF IMPAIRMENT AND SOCIODEMOGRAPHIC CORRELATES.**

**Ercan ES, Bilac O, Uysal OT, et al.**

This study was designed to assess the prevalence of psychiatric disorders and the impact of impairment criteria on rates of diagnoses in a representative sample of elementary school children from a country in a region. We sampled 419 primary school children by using a one-stage design in Izmir, Turkey. The response rate was 99.5 % and 417 cases were assessed using the Schedule for Affective Disorders and Schizophrenia for School-Age Children Present and Lifetime Version and a scale to assess the impairment criterion. The results showed that 36.7 % of the sample met DSM-IV criteria independent of impairment and that 14.1 % of the population had one or more DSM-IV disorders when a measure of impairment specific to each diagnosis was considered. The most prevalent disorders were attention-deficit/hyperactivity disorder and anxiety disorders. This study provided the first estimates of the prevalence of specific DSM-IV-defined psychiatric disorders in Turkish population of children.

Child Psychiatry Hum Dev. 2016 Feb;47:64-74.

**CLINICAL CORRELATES AND MEDIATORS OF SELF-CONCEPT IN YOUTH WITH CHRONIC TIC DISORDERS.**

**Hanks CE, McGuire JF, Lewin AB, et al.**

This study investigated the clinical correlates and mediators of self-concept in youth with Chronic Tic Disorders (CTD). Ninety-seven youth aged 6-17 (M = 11.1 +/- 2.89; 79.4 % male) with CTD were administered the Yale Global Tic Severity Scale, the Piers-Harris Children's Self-Concept Scale-Second



Edition, and self-report and clinician-administered measures assessing behavioral and psychological difficulties and comorbid conditions. Youth with CTD had a slightly below average level of self-concept, with 20 % (n = 19) exhibiting low self-concept. Youth with CTD-only had greater self-concept relative to youth with CTD and obsessive-compulsive disorder (OCD) (p = 0.04) or CTD, OCD, and attention deficit hyperactivity disorder (ADHD) combined (p = 0.009). Medium-to-large-sized associations were observed between youth's self-concept and clinical characteristics (e.g., severity of ADHD, OCD and depressive symptoms). Youth's self-concept partially mediated the relationship between tic severity and depressive symptom severity, and the interaction between tic impairment and youth's reliance on avoidant coping strategies moderated youth's self-concept. Implications, limitations, and recommendations for future interventions are discussed.

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Child Psychiatry Hum Dev. 2016 Feb;47:75-82.

**PRENATAL MATERNAL SMOKING AND TOURETTE SYNDROME: A NATIONWIDE REGISTER STUDY.**

**Leivonen S, Chudal R, Joelsson P, et al.**

This is the first nationwide register-based study to examine the relationship between prenatal maternal smoking and Tourette syndrome. A total of 767 children diagnosed with Tourette syndrome were identified from the Finnish Hospital Discharge Register. Each case was matched to four controls. Information on maternal smoking during pregnancy was obtained from the Finnish Medical Birth Register. Conditional logistic regression models were used for statistical analyses. Prenatal maternal smoking was associated with Tourette syndrome when comorbid with ADHD (OR 4.0, 95 % CI 1.2-13.5, p = 0.027 for exposure during first trimester, OR 1.7, 95 % CI, 1.05-2.7, p = 0.031 for exposure for the whole pregnancy). There was no association between maternal smoking during pregnancy and Tourette syndrome without comorbid ADHD (OR 0.5, 95 % CI 0.2-1.3, p = 0.166, OR 0.9, 95 % CI 0.7-1.3, p = 0.567). Further research is needed to elucidate the mechanisms behind the association between prenatal maternal smoking and Tourette syndrome with comorbid ADHD.

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Child Health Care. 2016;45:241-65.

**SCHOOL-BASED SCREENING TO IDENTIFY CHILDREN AT RISK FOR ATTENTION-DEFICIT/HYPERACTIVITY DISORDER: BARRIERS AND IMPLICATIONS.**

**Barry TD, Sturner R, Seymour K, et al.**

This report describes a school-based screening project to improve early identification of children at risk for attention-deficit/hyperactivity disorder (ADHD) and communicate these concerns to parents, recommending that they contact their child's primary care provider (PCP). Of 17,440 eligible children in first through fifth grades in five school districts, 47.0% of parents provided required written consent, and teachers completed 70.4% of the online screeners (using the Vanderbilt AD/HD Diagnostic Teacher Rating Scale). Of 5,772 screeners completed, 18.1% of children (n = 1,044) were identified as at risk. Parents of at-risk children were contacted to explain risk status and recommended to visit their child's PCP for further evaluation. It was not possible to contact 39.1% of parents of at-risk children. Of the 636 parents of at-risk children who could be contacted, 53.1% (n = 338) verbally accepted the recommendation to follow-up with their PCP, which was not related to ADHD symptom severity. Parents of children with IEPs or related services were more likely to accept the recommendation to visit the PCP. Our exploration of the potential for school-based screening for ADHD identified a number of barriers to successful execution, but the data also indicated that this is an important problem to address.

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Chin J Contemp Pediatr. 2016;18:496-500.

**EVENT-RELATED POTENTIAL AND BEHAVIORAL CHARACTERISTICS IN CHILDREN WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER OF DIFFERENT SCHOOL ENTRANCE AGES: A COMPARATIVE STUDY.**

**Shen HJ, Chen L, Zhao FQ, et al.**

**Objective:** To evaluate the effects of school entrance age on cognition and behaviors in children with attention deficit hyperactivity disorder (ADHD) using mathematical event-related potential (ERP), behavioral test, and Conners Parent Symptom Questionnaire (PSQ).

**Methods:** Fifty-eight ADHD children aged 7-12 years were enrolled and classified into older age and younger age groups according to the school entrance age (n=29 each). The children in the older age group were admitted at an age of 6 years and 6 months to 6 years and 11 months, and those in the younger age group were admitted at an age of 6 years to 6 years and 5 months. The ERP with a mathematical task was used to detect the difference in brain electrical activity between the two groups, and the behavioral test results were compared. The children's parents were asked to complete the PSQ, and the scores on each subscale were compared.

**Results:** The ERP detection showed that the older age group had a significantly higher P2 amplitude for wrong answers than the younger age group (10.9-5.0 ++v vs 8.5-3.6 ++v;  $P < 0.05$ ). The younger age group had a significantly shorter time of response to wrong answers than the older age group (619-340 ms vs 870-418 ms;  $P < 0.05$ ). The scores on the subscales of learning problems and impulse-hyperactivity of PSQ were significantly higher in the younger age group than in the older age group ( $P < 0.05$ ).

**Conclusions:** School entrance age can affect cognition and behaviors in children with ADHD, and the ADHD children with a younger school entrance age have an obvious defect in executive function, especially the function of error detection, which leads to the prominent problems in impulse-hyperactivity and learning.

Chin Med J. 2016;129:1922-28.

**COGNITIVE FUNCTION OF CHILDREN AND ADOLESCENTS WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER AND LEARNING DIFFICULTIES: A DEVELOPMENTAL PERSPECTIVE.**

**Huang F, Sun L, Qian Y, et al.**

**Background:** The cognitive function of children with either attention deficit hyperactivity disorder (ADHD) or learning disabilities (LDs) is known to be impaired. However, little is known about the cognitive function of children with comorbid ADHD and LD. The present study aimed to explore the cognitive function of children and adolescents with ADHD and learning difficulties in comparison with children with ADHD and healthy controls in different age groups in a large Chinese sample.

**Methods:** Totally, 1043 participants with ADHD and learning difficulties (the ADHD + learning difficulties group), 870 with pure ADHD (the pure ADHD group), and 496 healthy controls were recruited. To investigate the difference in cognitive impairment using a developmental approach, all participants were divided into three age groups (6-8, 9-11, and 12-14 years old). Measurements were the Chinese-Wechsler Intelligence Scale for Children, the Stroop Color-Word Test, the Trail-Making Test, and the Behavior Rating Inventory of Executive Function-Parents (BRIEF). Multivariate analysis of variance was used.

**Results:** The results showed that after controlling for the effect of ADHD symptoms, the ADHD+ learning difficulties group was still significantly worse than the pure ADHD group, which was, in turn, worse than the control group on full intelligence quotient (98.66 - 13.87 vs. 105.17 - 14.36 vs. 112.93 - 13.87,  $P < 0.001$ ). The same relationship was also evident for shift function (shifting time of the Trail-Making Test, 122.50 [62.00, 194.25] s vs. 122.00 [73.00, 201.50] s vs. 66.00 [45.00, 108.00] s,  $P < 0.001$ ) and everyday life executive function (BRIEF total score, 145.71 - 19.35 vs. 138.96 - 18.00 vs. 122.71 - 20.45,  $P < 0.001$ ) after controlling for the effect of the severity of ADHD symptoms, intelligence quotient, age, and gender. As for the age groups, the differences among groups became nonsignificant in the 12-14 years old group for inhibition (meaning interference of the Stroop Color-Word Test, 18.00 [13.00, 25.00] s vs. 17.00 [15.00, 26.00] s vs. 17.00 [10.50, 20.00] s,  $P = 0.704$ ) and shift function (shifting time of the Trail-Making Test, 62.00 [43.00, 97.00] s vs. 53.00 [38.00, 81.00] s vs. 101.00 [88.00, 114.00] s,  $P = 0.778$ ).

**Conclusions:** Children and adolescents with ADHD and learning difficulties have more severe cognitive impairment than pure ADHD patients even after controlling for the effect of ADHD symptoms. However, the

differences in impairment in inhibition and shift function are no longer significant when these individuals were 12-14 years old.

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Clin Drug Investig. 2016 Jan;36:1-25.

**GUANFACINE EXTENDED RELEASE: A NEW PHARMACOLOGICAL TREATMENT OPTION IN EUROPE.**

**Huss M, Chen W, Ludolph AG.**

Children/adolescents with attention-deficit/hyperactivity disorder (ADHD) may have a poor or inadequate response to psychostimulants or be unable to tolerate their side-effects; furthermore, stimulants may be inappropriate because of co-existing conditions. Only one non-stimulant ADHD pharmacotherapy, the noradrenaline transporter inhibitor atomoxetine, is currently approved for use in Europe. We review recent advances in understanding of the pathophysiology of ADHD with a focus on the roles of catecholamine receptors in context of the alpha2A-adrenergic receptor agonist guanfacine extended release (GXR), a new non-stimulant treatment option in Europe. Neuroimaging studies of children/adolescents with ADHD show impaired brain maturation, and structural and functional anomalies in brain regions and networks. Neurobiological studies in ADHD and medication response patterns support involvement of monoaminergic neurotransmitters (primarily dopamine and noradrenaline). Guanfacine is a selective alpha2A-adrenergic receptor agonist that has been shown to improve prefrontal cortical cognitive function, including working memory. The hypothesized mode of action of guanfacine centres on direct stimulation of post-synaptic alpha2A-adrenergic receptors to enhance noradrenaline neurotransmission. Preclinical data suggest that guanfacine also influences dendritic spine growth and maturation. Clinical trials have demonstrated the efficacy of GXR in ADHD, and it is approved as monotherapy or adjunctive therapy to stimulants in Canada and the USA (for children and adolescents). GXR was approved recently in Europe for the treatment of ADHD in children and adolescents for whom stimulants are not suitable, not tolerated or have been shown to be ineffective. GXR may provide particular benefit for children/adolescents who have specific co-morbidities such as chronic tic disorders or oppositional defiant disorder (or oppositional symptoms) that have failed to respond to first-line treatment options.

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Clin EEG Neurosci. 2016 Jan;47:56-60.

**BEHAVIORAL AND MOVEMENT DISORDERS DUE TO LONG-LASTING MYOCLONIC STATUS EPILEPTICUS MISDIAGNOSED AS ADHD IN A PATIENT WITH JUVENILE MYOCLONIC EPILEPSY: ELECTROCLINICAL FINDINGS AND RELATED HEMODYNAMIC CHANGES.**

**Fanella M, Carni M, Morano A, et al.**

Epilepsy and attention-deficit/hyperactivity disorder (ADHD) likely share common underlying neural mechanisms, as often suggested by both the evidence of electroencephalography (EEG) abnormalities in ADHD patients without epilepsy and the coexistence of these 2 conditions. The differential diagnosis between epilepsy and ADHD may consequently be challenging. In this report, we describe a patient presenting with a clinical association of "tics" and behavioral disorders that appeared 6 months before our first observation and had previously been interpreted as ADHD. A video-EEG evaluation documented an electroclinical pattern of myoclonic status epilepticus. On the basis of the revised clinical data, the EEG findings, the good response to valproate, the long-lasting myoclonic status epilepticus, and the enduring epileptic abnormalities likely causing behavioral disturbances, the patient's symptoms were interpreted as being the expression of untreated juvenile myoclonic epilepsy. The EEG-functional magnetic resonance imaging study revealed, during clinical generalized spike-and-wave and polyspike-and-wave discharges, positive blood oxygen level-dependent (BOLD) signal changes bilaterally in the thalamus, the prefrontal cortex (Brodmann area 6, supplementary motor area) and the cerebellum, and negative BOLD signal changes in the regions of the default mode network. Such findings, which are typical of BOLD changes observed in idiopathic generalized epilepsy, may also shed light on the anatomofunctional network underlying ADHD.

Clin Neurophysiol. 2016 Feb;127:1307-20.

**EEG ALPHA POWER DURING MAINTENANCE OF INFORMATION IN WORKING MEMORY IN ADULTS WITH ADHD AND ITS PLASTICITY DUE TO WORKING MEMORY TRAINING: A RANDOMIZED CONTROLLED TRIAL.**

*Liu ZX, Glizer D, Tannock R, et al.*

**OBJECTIVE:** The present study examined whether neural indices of working memory maintenance differ between young adults with ADHD and their healthy peers (Study 1), and whether this neural index would change after working memory training (Study 2).

**METHODS:** Study 1 involved 136 college students with ADHD and 41 healthy peers (aged 18-35 years) and measured their posterior alpha activity during a visual delayed-match-to-sample task using electroencephalography (EEG). Study 2 involved 99 of the participants with ADHD who were randomized into a standard-length or shortened-length Cogmed working memory training program or a waitlist control group.

**RESULTS:** The ADHD group tended to be less accurate than the peers. Similarly, the ADHD group exhibited lower posterior alpha power at a trend level compared to their healthy peers. There were no training effects on participants' performance and only marginal increases in posterior alpha power in training groups compared to the waitlist group.

**CONCLUSIONS:** Considering that the training effects were small and there was no load and dose effect, we conclude that the current study provides no convincing evidence for specific effects of Cogmed.

**SIGNIFICANCE:** These findings provide unique insights into neuroplasticity, or lack thereof, with near-transfer tasks in individuals with ADHD.

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Clin Neurophysiol. 2016 Feb;127:1196-205.

**CORRELATION OF EEG WITH NEUROPSYCHOLOGICAL STATUS IN CHILDREN WITH EPILEPSY.**

*Hsu DA, Rayer K, Jackson DC, et al.*

**OBJECTIVE:** To determine correlations of the EEG frequency spectrum with neuropsychological status in children with idiopathic epilepsy.

**METHODS:** Forty-six children ages 8-18 years old with idiopathic epilepsy were retrospectively identified and analyzed for correlations between EEG spectra and neuropsychological status using multivariate linear regression. In addition, the theta/beta ratio, which has been suggested as a clinically useful EEG marker of attention-deficit hyperactivity disorder (ADHD), and an EEG spike count were calculated for each subject.

**RESULTS:** Neuropsychological status was highly correlated with posterior alpha (8-15 Hz) EEG activity in a complex way, with both positive and negative correlations at lower and higher alpha frequency sub-bands for each cognitive task in a pattern that depends on the specific cognitive task. In addition, the theta/beta ratio was a specific but insensitive indicator of ADHD status in children with epilepsy; most children both with and without epilepsy have normal theta/beta ratios. The spike count showed no correlations with neuropsychological status.

**CONCLUSIONS:** (1) The alpha rhythm may have at least two sub-bands which serve different purposes. (2) The theta/beta ratio is not a sensitive indicator of ADHD status in children with epilepsy. (3) The EEG frequency spectrum correlates more robustly with neuropsychological status than spike count analysis in children with idiopathic epilepsy.

**SIGNIFICANCE:** (1) The role of posterior alpha rhythms in cognition is complex and can be overlooked if EEG spectral resolution is too coarse or if neuropsychological status is assessed too narrowly. (2) ADHD in children with idiopathic epilepsy may involve different mechanisms from those in children without epilepsy. (3) Reliable correlations with neuropsychological status require longer EEG samples when using spike count analysis than when using frequency spectra.

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CNS Drugs. 2016;1-12.

**A COST-UTILITY ANALYSIS OF LISDEXAMFETAMINE VERSUS ATOMOXETINE IN THE TREATMENT OF CHILDREN AND ADOLESCENTS WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER AND INADEQUATE RESPONSE TO METHYLPHENIDATE.**

**Zimovetz EA, Beard SM, Hodgkins P, et al.**

**Background:** An economic analysis from the perspective of the UK National Health Service (NHS) evaluated the cost effectiveness of lisdexamfetamine dimesylate (LDX) compared with atomoxetine in children and adolescents with attention-deficit/hyperactivity disorder who have had an inadequate response to methylphenidate.

**Methods:** A 1-year decision-analytic model was constructed, with the health outcomes “response”, “nonresponse”, and “unable to tolerate”. Clinical data were taken from a head-to-head, randomized controlled trial in inadequate responders to methylphenidate. Response to treatment was defined as a score of 1 (very much improved) or 2 (much improved) on the Clinical Global Impression–Improvement subscale. Tolerability was assessed by discontinuation rates owing to adverse events. Utility weights were identified via a systematic literature review. Healthcare resource use estimates were obtained via a survey of clinicians. Daily drug costs were derived from British National Formulary 2012 costs and mean doses reported in the trial. One-way and probabilistic sensitivity analyses (PSAs) were performed.

**Results:** The comparison of LDX with atomoxetine resulted in an estimate of an incremental cost-effectiveness ratio of £1802 per quality-adjusted life-year (QALY). The result was robust in a wide range of sensitivity analyses; results were most sensitive to changes in drug costs and efficacy. In the PSA, assuming a maximum willingness to pay of £20,000 per QALY, LDX versus atomoxetine had an 86 % probability of being cost effective. In 38 % of PSA runs, LDX was more effective and less costly than atomoxetine.

**Conclusions:** From the perspective of the UK NHS, LDX provides a cost-effective treatment option for children and adolescents who are inadequate responders to methylphenidate.

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Cochrane Database Syst Rev. 2016;CD005041.

**WITHDRAWN: IMMEDIATE-RELEASE METHYLPHENIDATE FOR ATTENTION DEFICIT HYPERACTIVITY DISORDER (ADHD) IN ADULTS.**

**Epstein T, Patsopoulos NA, Weiser M.**

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Cortex. 2016.

**DOUBLE-DISSOCIATION BETWEEN THE MECHANISM LEADING TO IMPULSIVITY AND INATTENTION IN ATTENTION DEFICIT HYPERACTIVITY DISORDER: A RESTING-STATE FUNCTIONAL CONNECTIVITY STUDY.**

**Sanefuji M, Craig M, Parlatini V, et al.**

Two core symptoms characterize Attention Deficit Hyperactivity Disorder (ADHD) subtypes: inattentiveness and hyperactivity-impulsivity. While previous brain imaging research investigated ADHD as if it was a homogenous condition, its two core symptoms may originate from different brain mechanisms. We, therefore, hypothesized that the functional connectivity of cortico-striatal and attentional networks would be different between ADHD subtypes. We studied 165 children (mean age 10.93 years; age range, 7-17 year old) diagnosed as having ADHD based on their revised Conner's rating scale score and 170 typical developing individuals (mean age 11.46 years; age range, 7-17 year old) using resting state functional fMRI. Groups were matched for age, IQ and head motion during the MRI acquisition. We fractionated the ADHD group into predominantly inattentive, hyperactive-impulsive and combined subtypes based on their revised Conner's rating scale score. We then analyzed differences in resting state functional connectivity of the cortico-striatal and attentional networks between these subtypes. We found a double dissociation of functional connectivity in the cortico-striatal and ventral attentional networks, reflecting the subtypes of the ADHD participants. Particularly, the hyperactive-impulsive subtype was associated with increased connectivity in cortico-striatal network, whereas the inattentive subtype was associated with increased connectivity in the right ventral attention network. Our study demonstrated for the first time a right lateralized, double dissociation between

specific networks associated with hyperactivity-impulsivity and inattentiveness in ADHD children, providing a biological basis for exploring symptom dimensions and revealing potential targets for more personalized treatments.

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Dev Med Child Neurol. 2016 Jan;58:16-28.

**NEUROPSYCHIATRIC MANIFESTATIONS OF SYDENHAM'S CHOREA: A SYSTEMATIC REVIEW.**

**Punukollu M, Mushet N, Linney M, et al.**

**AIM:** Sydenham's chorea is a post-streptococcal, autoimmune, neuropsychiatric movement disorder. Sydenham's chorea is a major criterion for diagnosis of acute rheumatic fever with the implication of potential long-term sequelae including cardiac complications. It is well established that there is psychiatric comorbidity in Sydenham's chorea, but there are variations in the literature regarding the nature and prevalence of psychiatric diagnoses associated with Sydenham's chorea. The aim of this review was to systematically evaluate the evidence for psychiatric symptoms presenting with Sydenham's chorea. Knowledge of comorbid psychiatric symptomatology will support early diagnosis and treatment, leading to improved long-term outcomes for children with Sydenham's chorea.

**METHOD:** The study used a systematic search strategy, using MEDLINE, MEDLINE in Process, EMBASE, and The Cochrane Library. Abstracts were screened to identify relevant papers which were then assessed further. Eligible papers were summarized.

**RESULTS:** A total of 1429 abstracts of relevant studies were found, and 49 papers reporting neuropsychiatric symptoms in Sydenham's chorea were summarized. Obsessive-compulsive disorder was the most commonly studied, and hence reported, neuropsychiatric symptom in children with Sydenham's chorea. The studies analysed used a variety of tools to identify affected children and used different methods for analysing results. Attention-deficit-hyperactivity disorder, affective disorders, tic disorders, executive function disturbances, and psychotic features were also reported as comorbidities.

**INTERPRETATION:** There is good evidence of neuropsychiatric comorbidities in Sydenham's chorea. In countries with a high prevalence of rheumatic fever, the early recognition of salient cognitive and psychiatric symptoms may aid in the management of Sydenham's chorea.

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Dev Period Med. 2016 Jan;20:75-81.

**POTENTIAL EFFECTS OF SCREEN MEDIA ON COGNITIVE DEVELOPMENT AMONG CHILDREN UNDER 3 YEARS OLD: REVIEW OF LITERATURE.**

**Brzozowska I, Sikorska I.**

The literature review regarding potential effects of screen media on cognitive development among children under 3 years old, is presented. In this article, cognitive aspects of development include acquisition of language, attention, learning and later school performance. The constant increase of children's access to television is noted, indicating that 60% of infants and toddlers watch TV regularly for 1-2 hours per day. The review included 40 articles and book chapters of significant such as Anderson, Barr, Christakis, Zimmerman, Meltzoff, Courage, Setliff, Troseth. The data was selected from electronic databases of scientific publications: Psychology & Behavioral Sciences Collection, Social Sciences Full Text (H.W. Wilson) and Humanities Full Text (H.W. Wilson) available in Poland. Cited articles provide evidence of the negative impact of exposure to television, media and video on the cognitive functioning of children under 3 years old. The potential impact of watching TV for difficulties in ability to focus attention appears as a core danger. Furthermore, studies suggest a possible connection between early exposure to television and ADHD as well as difficulties with language acquisition, learning and poorer school results.



Epidemiology and Psychiatric Sciences. 2016;1-11.

**PREVALENCE RATES OF YOUTHS DIAGNOSED WITH AND MEDICATED FOR ADHD IN A NATIONWIDE SURVEY IN TAIWAN FROM 2000 TO 2011.**

**Wang LJ, Lee SY, Yuan SS, et al.**

**Aims:** Public controversy regarding the potential overdiagnosis and overmedication of children with attention-deficit/hyperactivity disorder (ADHD) has continued for decades. This study used the National Health Insurance Research Database of Taiwan (NHIRD-TW) to explore trends in ADHD diagnosis in youths and the proportion of those receiving medication, with the aim of determining whether ADHD is overdiagnosed and overmedicated in Taiwan.

**Method:** Youths (age 7–18 years) who had at least two NHIRD-TW claims records with ADHD diagnosis between January 2000 and December 2011 were selected as the subject cohort. In total, the study sample comprised 145 018 patients with ADHD (mean age at a diagnosis of ADHD: 7.7 - 3.1 years; 21.4% females). The number of cases of ADHD were calculated annually for each year (from 2000 to 2011), and the number of cases per year who received medication was determined as those with at least one record of pharmacotherapy (immediate-release methylphenidate, osmotic controlled-release formulation of methylphenidate, and atomoxetine) in each year.

**Results:** The prevalence rates of a diagnosis of ADHD in the youths ranged from 0.11% in 2000 to 1.24% in 2011. Compared with children under 6 years of age, the ADHD diagnosis rates in children aged between 7 and 12 years (ratio of prevalence rates = 4.36) and in those aged between 13 and 18 years (ratio of prevalence rates = 1.42) were significantly higher during the study period. The prevalence in males was higher than that in females (ratio of prevalence rates = 4.09). Among the youths with ADHD, 50.2% received medications in 2000 compared with 61.0% in 2011. The probability of receiving ADHD medication increased with age. More male ADHD patients received medications than female patients (ratio of prevalence rates = 1.16).

**Conclusions:** The rate of ADHD diagnosis was far lower than the prevalence rate (7.5%) identified in a previous community study using face-to-face interviews. Approximately 40–50% of the youths with ADHD did not receive any medications. These findings are not consistent with a systematic public opinion about overdiagnosis or overmedication of ADHD in Taiwan.

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Eur Child Adolesc Psychiatry. 2016 Jan;25:17-23.

**THE DISCRIMINATIVE CAPACITY OF CBCL/1(1/2)-5-DSM5 SCALES TO IDENTIFY DISRUPTIVE AND INTERNALIZING DISORDERS IN PRESCHOOL CHILDREN.**

**De La Osa N, Granero R, Trepal E, et al.**

This paper studies the discriminative capacity of CBCL/1(1/2)-5 (Manual for the ASEBA Preschool-Age Forms & Profiles, University of Vermont, Research Center for Children, Youth, & Families, Burlington, 2000) DSM5 scales attention deficit and hyperactivity disorder (ADHD), oppositional defiant disorder (ODD), anxiety and depressive problems for detecting the presence of DSM5 (DSM5 diagnostic and statistical manual of mental disorders, APA, Arlington, 2013) disorders, ADHD, ODD, Anxiety and Mood disorders, assessed through diagnostic interview, in children aged 3-5. Additionally, we compare the clinical utility of the CBCL/1(1/2)-5-DSM5 scales with respect to analogous CBCL/1(1/2)-5 syndrome scales. A large community sample of 616 preschool children was longitudinally assessed for the stated age group. Statistical analysis was based on ROC procedures and binary logistic regressions. ADHD and ODD CBCL/1(1/2)-5-DSM5 scales achieved good discriminative ability to identify ADHD and ODD interview's diagnoses, at any age. CBCL/1(1/2)-5-DSM5 Anxiety scale discriminative capacity was fair for unspecific anxiety disorders in all age groups. CBCL/1(1/2)-5-DSM5 depressive problems' scale showed the poorest discriminative capacity for mood disorders (including depressive episode with insufficient symptoms), oscillating into the poor-to-fair range. As a whole, DSM5-oriented scales generally did not provide evidence better for discriminative capacity than syndrome scales in identifying DSM5 diagnoses. CBCL/1(1/2)-5-DSM5 scales discriminate externalizing disorders better than internalizing disorders for ages 3-5. Scores on the ADHD and ODD CBCL/1(1/2)-5-DSM5 scales can be used to screen for DSM5 ADHD and ODD disorders in general populations of preschool children.

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Eur Child Adolesc Psychiatry. 2016 Apr;25:453-54.

**A REPLY TO WANG T, SHAN L, DU L, FENG J, XU Z, STAAL WG, JIA F. SERUM CONCENTRATION OF 25-HYDROXYVITAMIN D IN AUTISM SPECTRUM DISORDER: A SYSTEMATIC REVIEW AND META-ANALYSIS. EUR CHILD ADOLESC PSYCHIATRY. 2015; DOI: 10.1007/s00787-015-0786-1.**

**Fluegge K.**

The author of this correspondence has recently published findings of an ecological investigation wherein herbicide use was proposed as an instrumental variable that predicts healthcare utilization among subjects with severe ADHD impairment via individual exposure to nitrous oxide (N<sub>2</sub>O) emissions. Vitamin D deficiency, a possible risk factor for autism spectrum disorders (ASD) as discussed by Wang et al., may be a homeostatic response to increasing chronic environmental N<sub>2</sub>O exposures. The author explains how deficient and insufficient states of vitamin D may promote vagal withdrawal and tolerance to increasing opioid exposures in the environment and how these characteristics are particularly relevant in neurodevelopmental disorders, like ASD and ADHD.

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Eur Child Adolesc Psychiatry. 2016 Feb;25:195-207.

**A CROSS-SECTIONAL STUDY TO ASSESS THE PREVALENCE OF DSM-5 SPECIFIC LEARNING DISORDERS IN REPRESENTATIVE SCHOOL SAMPLES FROM THE SECOND TO SIXTH GRADE IN BRAZIL.**

**Fortes IS, Paula CS, Oliveira MC, et al.**

Little is known about specific learning disorder (SLD) in low- and middle-income countries (LMICs), and even less from representative school samples in small size cities outside huge urban centers. Few studies addressed the new DSM-5 criteria for SLDs. We investigated the prevalence of DSM-5 SLDs, their comorbidities and correlates in school samples of students from the second to sixth grades living in median cities from four different geographic regions in Brazil. A national test for academic performance covering reading, writing and mathematical abilities was applied. Psychiatric diagnoses were assessed by the K-SADS-PL applied to the primary caregiver. A total of 1618 children and adolescents were included in the study. The following prevalence rates of SLDs were found: 7.6% for global impairment, 5.4% for writing, 6.0% for arithmetic, and 7.5% for reading impairment. Attention-deficit/hyperactivity disorder (ADHD) was the only comorbidity significantly associated with SLD with global impairment ( $p = 0.031$ ). Anxiety disorders and ADHD were associated with SLD with arithmetic impairment. Significant differences were detected in prevalence rates among cities, and several socio-demographic correlates (age, gender, IQ, and socioeconomic status) were significantly associated with SLD with global impairment in our sample. Careful validation and normalization of instruments to assess academic performance is a major problem in LMICs. As expected, we found a significant heterogeneity in prevalence rates of SLD according to geographic regions considering that Brazil is a country with a robust diversity. SLD with global and arithmetic impairment was significantly associated with psychiatric comorbidities.

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Eur Child Adolesc Psychiatry. 2016 Jan;25:25-31.

**OFF-LABEL PRESCRIBING OF PSYCHOTROPIC DRUGS IN A DANISH CHILD AND ADOLESCENT PSYCHIATRIC OUTPATIENT CLINIC.**

**Nielsen ES, Hellfritsch M, Sorensen MJ, et al.**

This study aimed to describe the level of off-label treatment with psychotropic drugs at a child and adolescent psychiatric outpatient clinic in Denmark. We performed a cross-sectional study assessing records on patients treated with medicine at two outpatient clinics at the child and adolescent psychiatric ward, on 1 day in 2014. Prescriptions of drugs from ATC group N05-N06 were classified according to label status. Six hundred and fifteen drug prescriptions distributed on nine different drugs were prescribed to 503 children eligible for this study. Overall results showed that 170 of the 615 prescriptions were off-label, which corresponds to 27.6 %. Attention deficit hyperkinetic disorder (ADHD) drugs were prescribed 450 times (73.2 %) of which 11 prescriptions were off-label (2.4 %). Other psychotropic drugs comprised 165 (26.8 %) prescriptions and of these 159 (96.4 %) were off-label. With 106 prescriptions, melatonin was the most prescribed of these drugs;

all prescriptions were off-label. The main reasons for classifying prescriptions as off-label were age and indication of treatment. This cross-sectional study reveals that medical treatment of children with other psychotropic drugs than ADHD drugs is usually off-label. ADHD drugs were, as the only drug group, primarily prescribed on-label. Although off-label prescription may be rational and even evidence based, the responsibility in case of, e.g. adverse drug reactions is a challenge, and clinical trials in children should be incited.

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Eur Child Adolesc Psychiatry. 2016 Jan;25:83-90.

**ATTENTION-DEFICIT/HYPERACTIVITY DISORDER DIMENSIONALITY: THE RELIABLE 'G' AND THE ELUSIVE 'S' DIMENSIONS.**

**Wagner F, Martel MM, Cogo-Moreira H, et al.**

The best structural model for attention-deficit/hyperactivity disorder (ADHD) symptoms remains a matter of debate. The objective of this study is to test the fit and factor reliability of competing models of the dimensional structure of ADHD symptoms in a sample of randomly selected and high-risk children and pre-adolescents from Brazil. Our sample comprised 2512 children aged 6-12 years from 57 schools in Brazil. The ADHD symptoms were assessed using parent report on the development and well-being assessment (DAWBA). Fit indexes from confirmatory factor analysis were used to test unidimensional, correlated, and bifactor models of ADHD, the latter including "g" ADHD and "s" symptom domain factors. Reliability of all models was measured with omega coefficients. A bifactor model with one general factor and three specific factors (inattention, hyperactivity, impulsivity) exhibited the best fit to the data, according to fit indices, as well as the most consistent factor loadings. However, based on omega reliability statistics, the specific inattention, hyperactivity, and impulsivity dimensions provided very little reliable information after accounting for the reliable general ADHD factor. Our study presents some psychometric evidence that ADHD specific ("s") factors might be unreliable after taking common ("g" factor) variance into account. These results are in accordance with the lack of longitudinal stability among subtypes, the absence of dimension-specific molecular genetic findings and non-specific effects of treatment strategies. Therefore, researchers and clinicians might most effectively rely on the "g" ADHD to characterize ADHD dimensional phenotype, based on currently available symptom items.

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Eur Child Adolesc Psychiatry. 2016;1-10.

**DECISION-MAKING IN SOCIAL CONTEXTS IN YOUTH WITH ADHD.**

**Ma I, Lambregts-Rommelse NNJ, Buitelaar JK, et al.**

This study examined reward-related decision-making in children and adolescents with ADHD in a social context, using economic games. We furthermore examined the role of individual differences in reward-related decision-making, specifically, the roles of reward sensitivity and prosocial skills. Children and adolescents (9-17 years) with ADHD-combined subtype (n = 29; 20 boys) and healthy controls (n = 38; 20 boys) completed the ultimatum game and dictator game as measures of reward-related decision-making in social contexts. Prosocial skills were measured with the Interpersonal Reactivity Index. The ADHD group had a larger discrepancy between ultimatum game and dictator game offers than controls, indicating strategic rather than fairness driven decisions. This finding was supported by self-reports showing fewer individuals with ADHD than controls who considered fairness as motive for the decisions. Perspective taking or empathic concern did not differ between groups and was not significantly associated with offers. In conclusion, the results suggest that rather than a failure to understand the perspective of others, children and adolescents with ADHD were less motivated by fairness than controls in simple social situations. Results encourage the use of economic games in ADHD research.

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Eur Child Adolesc Psychiatry. 2016;1-9.

**SERUM BRAIN-DERIVED NEUROTROPHIC FACTOR, GLIAL-DERIVED NEUROTROPHIC FACTOR, NERVE GROWTH FACTOR, AND NEUROTROPHIN-3 LEVELS IN CHILDREN WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.**

**Bilgiç A, Toker A, Işık Ü, et al.**

It has been suggested that neurotrophins are involved in the etiopathogenesis of attention-deficit/hyperactivity disorder (ADHD). This study aimed to investigate whether there are differences in serum brain-derived neurotrophic factor (BDNF), glial-derived neurotrophic factor (GDNF), nerve growth factor (NGF), and neurotrophin-3 (NTF3) levels between children with ADHD and healthy controls. A total of 110 treatment-naive children with the combined presentation of ADHD and 44 healthy controls aged 8–18 years were enrolled in this study. The severity of ADHD symptoms was determined by scores on the Conners' Parent Rating Scale-Revised Short and Conners' Teacher Rating Scale-Revised Short. The severity of depression and anxiety symptoms of the children were evaluated by the self-report inventories. Serum levels of neurotrophins were measured using commercial enzyme-linked immunosorbent assay kits. The multivariate analysis of covariance (MANCOVA) revealed a significant main effect of groups in the levels of serum neurotrophins, an effect that was independent of age, sex, and the severity of the depression and anxiety. The analysis of covariance (ANCOVA) indicated that the mean serum GDNF and NTF3 levels of ADHD patients were significantly higher than that of controls. However, serum BDNF and NGF levels did not show any significant differences between groups. No correlations between the levels of serum neurotrophins and the severity of ADHD were observed. These results suggest that elevated serum GDNF and NTF3 levels may be related to ADHD in children.

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Eur Neuropsychopharmacol. 2016.

**META-ANALYSIS OF THE DRD5 VNTR IN PERSISTENT ADHD.**

**Klein M, Berger S, Hoogman M, et al.**

Attention-Deficit/Hyperactivity Disorder (ADHD) is a common neuropsychiatric disorder with a complex genetic background. DRD5, the gene encoding the dopamine receptor D5, was recently confirmed as a candidate gene for ADHD in children through meta-analysis. In this study, we aimed at studying the association of the ADHD-associated variable number tandem repeat (VNTR) polymorphism upstream of DRD5 with adult ADHD. We compiled data from six sites of the International Multicentre persistent ADHD CollaboraTion (IMPACT) and reached N=6979 (3344 cases and 3635 healthy participants), the largest sample investigated so far. We tested the association of the common DRD5 alleles with categorically defined ADHD and with inattentive and hyperactive/impulsive symptom counts. Our findings provide evidence that none of the common DRD5 alleles are associated with ADHD risk or ADHD symptom counts in adults.

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Front Psychiatry. 2016;7.

**MULTIVARIATE IMAGING GENETICS STUDY OF MRI GRAY MATTER VOLUME AND SNPs REVEALS BIOLOGICAL PATHWAYS CORRELATED WITH BRAIN STRUCTURAL DIFFERENCES IN ATTENTION DEFICIT HYPERACTIVITY DISORDER.**

**Khadka S, Pearlson GD, Calhoun VD, et al.**

**Background:** Attention deficit hyperactivity disorder (ADHD) is a prevalent neurodevelopmental disorder affecting children, adolescents, and adults. Its etiology is not well understood, but it is increasingly believed to result from diverse pathophysiologies that affect the structure and function of specific brain circuits. Although one of the best-studied neurobiological abnormalities in ADHD is reduced fronto-striatal-cerebellar gray matter (GM) volume, its specific genetic correlates are largely unknown.

**Methods:** In this study, T1-weighted MR images of brain structure were collected from 198 adolescents (63 ADHD-diagnosed). A multivariate parallel independent component analysis (Para-ICA) technique-identified imaging genetic relationships between regional GM volume and single nucleotide polymorphism data.

**Results:** Para-ICA analyses extracted 14 components from genetic data and 9 from MR data. An iterative cross-validation using randomly chosen subsamples indicated acceptable stability of these ICA solutions. A series of partial correlation analyses controlling for age, sex, and ethnicity revealed two genotype-phenotype

component pairs significantly differed between ADHD and non-ADHD groups, after a Bonferroni correction for multiple comparisons. The brain phenotype component not only included structures frequently found to have abnormally low volume in previous ADHD studies but was also significantly associated with ADHD differences in symptom severity and performance on cognitive tests frequently found to be impaired in patients diagnosed with the disorder. Pathway analysis of the genotype component identified several different biological pathways linked to these structural abnormalities in ADHD.

**Conclusion:** Some of these pathways implicate well-known dopaminergic neurotransmission and neurodevelopment hypothesized to be abnormal in ADHD. Other more recently implicated pathways included glutamatergic and GABA-ergic physiological systems; others might reflect sources of shared liability to disturbances commonly found in ADHD, such as sleep abnormalities.

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Front Psychol. 2016 Jul;7.

**CHILDREN WITH ATTENTION DEFICIT/HYPERACTIVITY DISORDER AND READING DISABILITY: A REVIEW OF THE EFFICACY OF MEDICATION TREATMENTS.**

**Gray C, Climie EA.**

Reading is a multifaceted skillset that has the potential to profoundly impact a child's academic performance and achievement. Mastery of reading skills is often an area of difficulty for children during their academic journey, particularly for children with Attention Deficit/Hyperactivity Disorder (ADHD), Specific Learning Disorder with Impairment in Reading (SLD-R), or children with a comorbid diagnosis of both ADHD and SLD-R. ADHD is characterized by executive functioning and impulse control deficits, as well as inattention and impulsivity. Among the academic struggles experienced by children with ADHD are challenges with word reading, decoding, or reading comprehension. Similarly, children with SLD-R frequently encounter difficulties in the development of appropriate reading skills. SLD-R incorporates dysfunctions in basic visual and auditory processes that result in difficulties with decoding and spelling words. There have been limited empirical studies investigating the efficacy of interventions to improve the reading ability of children with both ADHD and SLD-R. Research studies that have focused on reading interventions for children from this population have predominantly included the use of medication treatments with stimulants (e.g., methylphenidate) and non-stimulants (e.g., atomoxetine). This review paper will present and integrate findings from empirical studies on successful medication treatments for children with comorbid ADHD and SLD-R. Furthermore, this paper will extend findings from empirically successful medication treatments to provide directions for future research.

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Genes Brain Behav. 2016.

**INTERPLAY BETWEEN STRESS RESPONSE GENES ASSOCIATED WITH ATTENTION-DEFICIT HYPERACTIVITY DISORDER AND BRAIN VOLUME.**

**Van Der Meer D, Hoekstra PJ, Bralten J, et al.**

The glucocorticoid receptor plays a pivotal role in the brain's response to stress; a haplotype of functional polymorphisms in the NR3C1 gene encoding this receptor has been associated with attention-deficit hyperactivity disorder (ADHD). The serotonin transporter (5-HTT) gene polymorphism 5-HTTLPR is known to influence the relation between stress exposure and ADHD severity, which may be partly because of its reported effects on glucocorticoid levels. We therefore investigated if NR3C1 moderates the relation of stress exposure with ADHD severity and brain structure, and the potential role of 5-HTTLPR. Neuroimaging, genetic and stress exposure questionnaire data were available for 539 adolescents and young adults participating in the multicenter ADHD cohort study NeuroIMAGE (average age: 17.2years). We estimated the effects of genetic variation in NR3C1 and 5-HTT, stress exposure and their interactions on ADHD symptom count and gray matter volume. We found that individuals carrying the ADHD risk haplotype of NR3C1 showed significantly more positive relation between stress exposure and ADHD severity than non-carriers. This gene-environment interaction was significantly stronger for 5-HTTLPR L-allele homozygotes than for S-allele carriers. These two- and three-way interactions were reflected in the gray matter volume of the cerebellum,

parahippocampal gyrus, intracalcarine cortex and angular gyrus. Our findings illustrate how genetic variation in the stress response pathway may influence the effects of stress exposure on ADHD severity and brain structure. The reported interplay between NR3C1 and 5-HTT may further explain some of the heterogeneity between studies regarding the role of these genes and hypothalamic-pituitary-adrenal axis activity in ADHD.

Harefuah. 2016 May;155:276-80, 323.

**DEMOGRAPHIC AND ANATOMIC CHARACTERISTICS AND SURGERY RESULTS IN CHILDREN WHO WERE TREATED IN SOROKA FOR CRANIOSYNOSTOSIS.**

**Perets O, Perry ZH, Rosenberg L, et al.**

**BACKGROUND:** Craniosynostosis, the premature fusion of one or more of the cranial sutures, can occur as a part of a syndrome or as an isolated deformity. When not treated properly it may have major physical and social implications.

**STUDY HYPOTHESIS:** We assumed that our center's results are similar to those reported in the literature, in terms of gender and anatomic characteristics, and different in terms of the number of syndromic cases. We also assume that only a few patients needed a second surgery and that this medical problem effects quality of life in term of cognitive impairment and aesthetic results.

**METHODS:** A retrospective chart review was conducted of patients who were treated for craniosynostosis in Soroka University Medical Center between the years 1991-2005.

**RESULTS:** A total of 63 patients were treated in Soroka during those years: 30 (47.6%) were females and 33 (50.8%) were males; 27 (42.9%) had coronal synostosis, 20 (31.8%) had sagital synostosis, 10 (15.8%) had metopic synostosis, 5 (7.9%) had lambdoid synostosis. A total of 5 (7.9%) cases were syndromic and the rest were isolated; 6 patients (9.5%) needed a second surgery for correction of the defect; 8 out of 30 patients (26.7%) 6 years or older at the present time suffer from attention deficit disorder. Parents' satisfaction from aesthetic results on a scale of 1-5 was 4.77 with SD of 0.504, while the doctors' score was 3.93 with SD 0.980 ( $p = 0.01$ ).

**CONCLUSIONS:** Craniosynostosis is a complex surgical problem, however with prompt treatment it may attain high levels of satisfaction among parents and patients. We found high rates 26.7% vs 10% (in the general population) of ADD in children affected by the disease.

Indian Journal of Clinical Biochemistry. 2016;1-7.

**A PRELIMINARY STUDY ON INVESTIGATION OF SERUM A-SYNUCLEIN AND TAU PROTEIN LEVELS IN CHILDREN WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER.**

**Cetin I, Simsek S.**

Neurodegenerative molecules play an important role in maintaining a supply for synaptic vesicles; and they are also likely to help regulate the dopamine release which is the primary mechanism of action in pharmacological treatments for attention deficit hyperactivity disorder (ADHD). It is suggested that there could be interactions between  $\alpha$ -synuclein and tau in cytoskeletal disorganization and synaptic dystrophy. Therefore, we aim to determine the serum levels of neurodegenerative molecules such as  $\alpha$ -synuclein and tau in children with ADHD. The study group consisted of 25 children, aged 6–10, diagnosed with ADHD according to DSM-IV criteria and who appeared at Dicle University, Faculty of Medicine, and Department of Child Psychiatry in Diyarbakir, Turkey. 25 children, having no psychiatric disorders and medical illnesses, were selected as healthy control group. Serum  $\alpha$ -synuclein and tau concentrations were determined by Enzyme-Linked Immuno Sorbent Assay. The  $\alpha$ -synuclein levels of ADHD were not significantly different than those of controls. The tau levels of ADHD were found to be statistically significantly higher than those of controls. Moreover,  $\alpha$ -synuclein levels showed a statistically significantly positive correlation with tau levels in children with ADHD. The results of our preliminary study can suggest that ADHD might possibly share a common disease mechanism with other diseases in terms of tau pathology. Increased serum tau level may be an indication of disturbance of microtubule transportation in the brains of children with ADHD.



Infant Child Dev. 2016 Jul;25:339-51.

**PRENATAL SMOKE EXPOSURE PREDICTS HYPERACTIVE/IMPULSIVE BUT NOT INATTENTIVE ADHD SYMPTOMS IN ADOLESCENT AND YOUNG ADULT GIRLS.**

**Gard AM, Owens EB, Hinshaw SP.**

We examined the longitudinal associations between prenatal tobacco smoke exposure (PSE) and attention-deficit hyperactivity disorder (ADHD) symptom domains in adolescence and young adulthood. A sample of girls with ADHD combined presentation (N = 93), ADHD predominantly inattentive presentation (N = 47), and matched comparisons (N = 88) was assessed prospectively. Symptoms of hyperactivity/impulsivity (HI), inattention (IA), and oppositionality (oppositional defiant disorder) were measured via multiple informants 5 (M age = 14 years; retention rate = 92%) and 10 years (M age = 20 years; retention rate = 95%) following childhood ascertainment. PSE was captured via maternal self-report. We used linear regressions to examine the prediction from PSE to both HI and IA in adolescence and early adulthood after stringent control of relevant confounding variables. PSE significantly predicted HI during adolescence and young adulthood across multiple informants but did not predict IA at either wave. Symptoms of HI may have partial etiological independence from IA symptoms

International Journal of Developmental Disabilities. 2016;1-9.

**PARENT-CHILD RELATIONSHIP AND BEHAVIOR PROBLEMS IN CHILDREN WITH ADHD.**

**Climie EA, Mitchell K.**

**Objectives:** Previous studies have examined the effect of parent-child relationships on conduct problems, but rarely are the mother-child and father-child relationships studied independently. The current study examined parent-child relationships and their connection to comorbid behaviors in children with Attention-Deficit/Hyperactivity Disorder (ADHD). More specifically, this study explored the mother-child and father-child relationship in children with ADHD, with an explicit focus on the aspects of the parent-child relationship that are related to more positive behavioral outcomes.

**Methods:** A sample of 74 children with ADHD (aged 8-11 years) and their mothers (n = 74) and fathers (n = 37) participated in the current study and completed a variety of parenting and behavioral measures. A number of relationship factors, including parent- and child-reported levels of attachment were examined in connection to parental ratings of behavioral outcomes such as defiance, aggression, and conduct problems.

**Results:** Results indicated that different aspects of the parent-child relationship for mothers and fathers were related to ratings of behavioral problems. Relational frustration was found to be a consistent predictor of negative ratings of behavior for both parents, while involvement was a predictor of more positive ratings of behavior for fathers only.

**Conclusions:** A better understanding of the specific aspects of the mother-child and father-child relationship may play a role in helping to understand the link between parent-child relationships and behavioral concerns in children with ADHD. Implications for practice are highlighted with a particular emphasis on strengthening the parent-child bond in families with children with ADHD.

International Journal of Pharmaceutical and Clinical Research. 2016;8:671-75.

**ROLE OF PLASMA FATTY ACIDS IN EGYPTIAN CHILDREN WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER.**

**Meguid N, Effat S, Hussien H, et al.**

The present study aimed to assess the effectiveness of n-3 PUFA supplementation on ADHD clinical symptoms and its tolerability in a randomized controlled study on Egyptian children. Vigil continuous performance test and Conners' questionnaires were used to assess changes in ADHD symptoms in 40 children; another 40 matched children were included in the study as controls. Supplements rich in EPA, DHA were randomly allocated for 4 months for only 20 cases. Plasma omega-3 fatty acids (eicosapentaenoic and docosahexaenoic acids) were assessed using Tandem Mass Spectrometry. The results revealed low levels of plasma omega-3 fatty acids were noted in children with ADHD compared to controls. Supplementation with n-3 PUFA resulted in significant increase in plasma EPA, DHA in children with ADHD. No adverse effects



were detected after n-3 PUFA supplement. According to parent version of the Conners' questionnaire improvement in symptoms was observed but it was not statistically significant except for the subscale measuring inattention. We concluded that Egyptian children with ADHD exhibited low levels of omega-3 fatty acids in polar lipids isolated from their plasma and are inversely correlated with degree of inattention. Our results support n-3 PUFA safety and tolerability and appear to be effective in alleviating symptoms of inattention.

Int J Technol Assess Health Care. 2016;1-8.

**TOP TEN RESEARCH PRIORITIES FOR ATTENTION DEFICIT/HYPERACTIVITY DISORDER TREATMENT.**

**Jacobson S, Östlund P, Wallgren L, et al.**

**Objectives:** The aim of this project was to identify the ten most important research questions for attention deficit/hyperactivity disorder (ADHD) treatment as identified by people with ADHD together with personnel involved in the treatment of ADHD in school, health, and correction services.

**Methods:** A working group consisting of consumers and personnel was established. The method for prioritization was primarily based on James Lind Alliance's guidebook, consisting of an interim priority setting exercise and a workshop.

**Results:** The top ten list includes the risk of drug dependency later in life when treated with methylphenidate as a child, teacher support, multimodal therapy, comparisons between atomoxetine and methylphenidate, methylphenidate treatment in substance abusers, parental support programmes, supported conversation, computer-aided working memory training, psychoeducative treatment, and melatonin.

**Conclusions:** We have shown that consumers and personnel can reach consensus on research priorities for treatments for ADHD. We encourage researchers and funders to consider the list for future studies.

Isr Med Assoc J. 2016 Jun;18:322-25.

**CLINICAL PROFILE OF ATTENTION DEFICIT HYPERACTIVITY DISORDER: IMPACT OF ETHNIC AND SOCIAL DIVERSITIES IN ISRAEL.**

**Mahaj M, Sharkia R, Shorbaji N, et al.**

**BACKGROUND:** Despite the increased worldwide recognition of attention deficit/hyperactivity disorder (ADHD), there is a variability in the diagnostic rate of both ADHD and its co-morbidities. These diversities are probably related to the methodology and instruments used for the diagnosis of ADHD and to awareness and cultural interpretation of its existence.

**OBJECTIVES:** To identify consistent differences in the clinical profile of Arab and Jewish children with ADHD in Israel who differ in cultural, ethnic and socioeconomic background.

**METHODS:** We analyzed the data of 823 children and adolescents with ADHD (516 Jews and 307 Arabs) and compared the clinical characteristics between these two ethnic groups. All patients were evaluated in two neuropsychiatric and child development centers in northern Israel: one in Haifa and one in Hadera. Children with autism and intellectual disabilities were excluded.

**RESULTS:** The distribution of ADHD subtypes was similar in both populations. However, learning disorders and psychiatric co-morbidities (behavioral difficulties and anxiety) were reported more frequently in the Jewish population. The most commonly reported adverse effects to psychostimulants were mood changes, anorexia, headache, insomnia and rebound effect, and were more frequently reported in the Jewish population (42.0% vs.18.0%,  $P < 0.05$ ).

**CONCLUSIONS:** We assume that these differences are related to cultural and socioeconomic factors. We suggest that the physician take cultural background into consideration when treating patients with ADHD.

J Affect Disord. 2016 Jan;190:508-16.

**COMORBIDITY VARIATION IN PATIENTS WITH OBSESSIVE-COMPULSIVE DISORDER ACCORDING TO SYMPTOM DIMENSIONS: RESULTS FROM A LARGE MULTICENTRE CLINICAL SAMPLE.**

**Torres AR, Fontenelle LF, Shavitt RG, et al.**

**BACKGROUND:** Obsessive-compulsive disorder (OCD) has a heterogeneous and complex phenomenological picture, characterized by different symptom dimensions and comorbid psychiatric disorders, which frequently co-occur or are replaced by others over the illness course. To date, very few studies have investigated the associations between specific OCD symptom dimensions and comorbid disorders.

**METHODS:** Cross-sectional, multicenter clinical study with 1001 well-characterized OCD patients recruited within the Brazilian Research Consortium on Obsessive-Compulsive and Related Disorders. The primary instruments were the Dimensional Yale-Brown Obsessive Compulsive Scale (DY-BOCS) and the Structured Clinical Interview for DSM-IV Axis I Disorders. Bivariate analyses between symptom dimensions and comorbidities were followed by logistic regression.

**RESULTS:** The most common comorbidities among participants (56.8% females) were major depression (56.4%), social phobia (34.6%), generalized anxiety disorder (34.3%), and specific phobia (31.4%). The aggressive dimension was independently associated with posttraumatic stress disorder (PTSD), separation anxiety disorder, any impulse-control disorder and skin picking; the sexual-religious dimension was associated with mood disorders, panic disorder/agoraphobia, social phobia, separation anxiety disorder, non-paraphilic sexual disorder, any somatoform disorder, body dysmorphic disorder and tic disorders; the contamination-cleaning dimension was related to hypochondriasis; and the hoarding dimension was associated with depressive disorders, specific phobia, PTSD, impulse control disorders (compulsive buying, skin picking, internet use), ADHD and tic disorders. The symmetry-ordering dimension was not independently associated with any comorbidity.

**LIMITATIONS:** Cross-sectional design; participants from only tertiary mental health services; personality disorders not investigated.

**CONCLUSIONS:** Different OCD dimensions presented some specific associations with comorbid disorders, which may influence treatment seeking behaviors and response, and be suggestive of different underlying pathogenic mechanisms.

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J Affect Disord. 2016 Jan;190:294-99.

**CHILDHOOD MOTOR COORDINATION AND ADULT PSYCHOPATHOLOGY IN EXTREMELY LOW BIRTH WEIGHT SURVIVORS.**

**Poole KL, Schmidt LA, Missiuna C, et al.**

**OBJECTIVE:** To determine if childhood motor coordination is associated with lifetime major depressive disorder (MDD), current generalized anxiety disorder (GAD), and attention-deficit/hyperactivity disorder (ADHD) in adulthood, and to examine if extremely low birth weight (ELBW; <1000 g) status moderates the strength of these associations.

**METHOD:** Prospective study of a cohort of normal birth weight (NBW) controls and ELBW survivors. Participants completed the short form Bruininks-Oseretsky Test of Motor Proficiency (BOTMP-SF) at age 8. At age 29-36, participants completed the Mini International Neuropsychiatric Interview to diagnose the psychiatric disorders of interest.

**RESULTS:** Birth weight status significantly influenced the strength and direction of associations between childhood motor coordination and adult psychiatric outcomes such that the odds of MDD (Pinteraction=.02) and GAD (Pinteraction=.01) increased with worsening motor scores in NBW adults but not ELBW survivors. Stratified analyses indicated that in NBW adults, for each one-point decrease in BOTMP-SF score, the odds of lifetime MDD increased by 10% (OR=1.10, 95% CI: 1.01-1.20).

**LIMITATIONS:** Participant attrition reduced sample size and that may have limited our ability to detect statistically significant results for some of our analyses.

**CONCLUSION:** Poorer motor coordination in early life has a negative long-term impact on the development

of MDD and GAD of individuals born at NBW. The long-term mental health risks of childhood motor coordination problems are significant and highlight the importance of recognizing motor deficits in all children, so that associated psychological difficulties can be identified and treated at an early age.

J Atten Disord. 2016 Jan;20:53-62.

**POSITIVE AND NEGATIVE AFFECT IN CLINIC-REFERRED YOUTH WITH ADHD.**

*Okado I, Mueller CW, Nakamura BJ.*

**OBJECTIVE:** To examine self-reported positive affect (PA) and negative affect (NA) among youth with ADHD (only and comorbid) and other non-ADHD-referred youth in an ethnically diverse clinical sample.

**METHOD:** Semi-structured interviews identified 80 pure ADHD, 284 ADHD plus one or more comorbidities, and 730 non-ADHD youth (e.g., other diagnoses or no diagnosis). The Positive and Negative Affect Scale-Children (PANAS-C) was used to assess affective states.

**RESULTS:** Even after controlling for the influence of potential confounds, youth with only ADHD reported higher PA and lower NA than other clinic-referred youth. The ADHD-comorbid group reported higher PA than the "non-ADHD" group, but these groups did not differ on level of NA. ADHD subtype did not influence results.

**CONCLUSION:** Among clinic-referred youth, ADHD is associated with higher levels of PA and when there are no comorbid disorders, lower levels of NA.

J Atten Disord. 2016 Jan;20:63-70.

**ENVIRONMENTAL STIMULATION DOES NOT REDUCE IMPULSIVE CHOICE IN ADHD: A "PINK NOISE" STUDY.**

*Metin B, Roeyers H, Wiersema JR, et al.*

**OBJECTIVE:** The preference for sooner smaller over larger later rewards is a prominent manifestation of impulsivity in ADHD. According to the State Regulation Deficit (SRD) model, this impulsive choice is the result of impaired regulation of arousal level and can be alleviated by adding environmental stimulation to increase levels of arousal.

**METHOD:** To test this prediction, we studied the effects of adding background "pink noise" on impulsive choice using a classical and new adjusting choice delay task in a sample of 25 children with ADHD and 28 controls.

**RESULTS:** Children with ADHD made more impulsive choices than controls. Adding noise did not reduce impulsive choice in ADHD.

**CONCLUSION:** The findings add to the existing evidence on impulsive choice in ADHD, but no evidence is found for the SRD model's explanation of this behavioral style. Alternative explanations for impulsive choice in ADHD are discussed.

J Atten Disord. 2016 Jan;20:43-52.

**DISPOSITIONAL TRAIT TYPES OF ADHD IN YOUNG CHILDREN.**

*Martel MM.*

**OBJECTIVE:** This study evaluated a novel person-centered approach to parsing ADHD heterogeneity using dispositional traits.

**METHOD:** Participants were one hundred nine 3- to 6-year-olds, and their primary caregivers and day care providers/teachers who completed a multi-informant diagnostic procedure with longitudinal follow-up.

**RESULTS:** Based on latent profile analysis, young children with ADHD could be divided into low control, high surgency, and high negative affect subgroups. The low control and high surgency groups exhibited increased parent- and teacher-rated hyperactive-impulsive and oppositional-defiant disorder (ODD) symptoms. Although the low control group exhibited the worst response inhibition, the high surgency group exhibited the worst working memory. Furthermore, the high surgency group exhibited high aggression and increasing levels of hyperactivity-impulsivity and ODD symptoms over time.

**CONCLUSION:** A subgroup of young children with ADHD with high surgency may be at particular risk for comorbid psychopathology and longitudinal worsening of symptoms.

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J Atten Disord. 2016 Jan;20:71-81.

**THE IMPACT OF IDLE TIME IN THE CLASSROOM: DIFFERENTIAL EFFECTS ON CHILDREN WITH ADHD.**

*Imeraj L, Antrop I, Roeyers H, et al.*

**OBJECTIVE:** Studies have identified an exacerbation of ADHD deficits under specific laboratory conditions. Less is known about the significance of such contextual factors in relation to everyday functioning in naturalistic settings.

**METHOD:** This study investigated the differential impact of classroom "idle time"-periods when students are not actively engaged or waiting for a task--on the behavior of 31 children with ADHD (25 boys and 6 girls; aged 6-12 years) and 31 sex- and age-matched typically developing classmates, who were simultaneously observed in their normal classroom during two school days.

**RESULTS:** Both groups experienced the same amount of idle time (12% of the time). During idle time, however, levels of hyperactivity and noisiness increased significantly more in children with ADHD than in their classmates ( $p < .05$ ).

**CONCLUSION:** Findings highlight the differential susceptibility of ADHD children to classroom idle time. Classroom interventions might consider targeting specifically these periods to reduce disruptive behavior in these children.

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J Atten Disord. 2016 Jan;20:21-33.

**BEHAVIORAL AND ACADEMIC PROGRESS OF CHILDREN DISPLAYING SUBSTANTIVE ADHD BEHAVIORS IN SPECIAL EDUCATION: A 1-YEAR FOLLOW-UP.**

*Stoutjesdijk R, Scholte EM, Swaab H.*

**OBJECTIVE:** Exploring differences in behavioral and academic progress between children displaying substantive ADHD behaviors (M age of 9.4 years) in special schools ( $n = 38$ ) and in inclusive education ( $n = 26$ ). The contribution of pedagogical strategies to positive outcomes was also examined.

**METHOD:** Measurements used were the Teachers' Report Form, the Social Emotional Questionnaire, assessments of academic achievement, and the Pedagogical Methods Questionnaire. Mixed-model ANOVAs and Pearson's correlations were used to analyze the data.

**RESULTS:** Significant progress was found regarding disorder-specific problem behavior and in all academic areas, but no interaction effect was found between time and setting. Correlations indicated that positive behavior reinforcement and emotional support are the pedagogical strategies that contributed most to behavioral adaptation.

**CONCLUSION:** Children displaying substantive ADHD behaviors in both groups develop equally well in the areas of behavioral and academic functioning where significant progress was found.

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J Atten Disord. 2016 Jan;20:34-40.

**RELATIONSHIP BETWEEN SLEEP PROBLEMS AND QUALITY OF LIFE IN CHILDREN WITH ADHD.**

*Yurumez E, Kilic BG.*

**OBJECTIVE:** The purpose of this study is to assess the sleep behaviors, sleep problems and frequency, and relationship with psychiatric comorbidities in ADHD Combined type and to evaluate the effect of sleep problems on quality of life.

**METHOD:** Forty-six boys, aged 7 to 13 years, with ADHD-combined type and 31 healthy boys were included. ADHD children were never treated for sleep or psychiatric disorders. Intelligence quotient (IQ) test scores were minimum 80, body mass index were normal and did not have medical disorders. Parents completed Children's Sleep Habits Questionnaire, Conners' Parent Rating Scale and The Pediatric Quality of Life

Inventory (PedsQL) and participants were asked about sleep behaviors and were administered PedsQL and Schedule for Affective Disorders and Schizophrenia.

**RESULTS:** The frequency of sleep problems in ADHD is 84.8%, higher than the control group ( $p = .002$ ). Evaluating PedsQL scores, the quality of life is worse in physical, psychosocial health, and total life quality ( $p < .05$ ). ADHD group with sleep problems have more night wakings than control group with sleep problems ( $p = .02$ ). The comorbidity do not increase sleep problems. The frequency of parasomnias is increased in group with learning disorders ( $p = .05$ ).

**CONCLUSION:** The results of this study, which controls for a number of possible confounders found in previous examinations of ADHD and sleep, support the results of a number of other studies that have found an increased overall prevalence of parent-reported sleep disturbances in children with ADHD compared with healthy control participants. As the ADHD group have more night wakings than the control group through the night, it is thought that night wakings that cause a partitioned sleep may be important signs seen in ADHD. That could be suggested by two hypotheses. First one is that, daytime sleepiness is more common in ADHD and those children present excessive hyperactivity during the day to stay awake and the second one is the improvement of ADHD signs when the drugs for sleepiness are used. Usage of standardized and valid diagnostic criteria, exclusion of adolescence, gender, socioeconomic level, primary sleep problems, medical disorders and low IQ level, making allowances for effect of comorbidities and having compared with the control group are the important methodological features of this study. The most important limitation of this study is small sample size that makes the findings less generalizable to other groups of children with ADHD, and another one is not having used objective measurements together with subjective measurements. In conclusion, these results underscore the importance of screening all children who have a symptom constellation suggestive of ADHD for sleep problems that may either play a causative role or exacerbate the clinical appearance of ADHD in a given child. Correct evaluation and treatment of sleep problems increase the life quality of family and child and also decrease the severity of ADHD symptoms.

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J Atten Disord. 2016 Jan;20:41-42.

**OBSTRUCTIVE SLEEP APNEA MIMICS ATTENTION DEFICIT DISORDER.**

**Blesch L, Breese McCoy SJ.**

Attention deficit and hyperactivity are known possible symptoms or correlates of obstructive sleep apnea (OSA). However, these associations may be missed in children, because children often fail to report excessive daytime sleepiness, and attention deficit disorder (ADD) and attention deficit hyperactivity disorder (ADHD) are common primary diagnoses in themselves. We report on a 17-year-old, slender, non-snoring male who presented to his pediatrician with a prolonged history of four complaints: inattention, fidgeting, frequent sinusitis, and somnolence. He was diagnosed with ADHD, while the somnolence, which often abated somewhat upon use of antibiotics for sinusitis, was attributed to the sinus infections. A later sleep study revealed OSA, and thorough additional testing proved that the original ADHD diagnosis was in error. All four conditions were allayed with proper use of a continuous positive airway pressure (CPAP) machine.

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J Autism Dev Disord. 2016 Jan;46:74-82.

**BOYS WITH ASPERGER SYNDROME GROW UP: PSYCHIATRIC AND NEURODEVELOPMENTAL DISORDERS 20 YEARS AFTER INITIAL DIAGNOSIS.**

**Gillberg IC, Helles A, Billstedt E, et al.**

We examined comorbid psychiatric and neurodevelopmental disorders in fifty adult males (mean age 30 years) with Asperger syndrome (AS) diagnosed in childhood and followed up prospectively for almost two decades (13-26 years). Only three of the 50 men had never met criteria for an additional psychiatric/neurodevelopmental diagnosis and more than half had ongoing comorbidity (most commonly either ADHD or depression or both). Any psychiatric comorbidity increased the risk of poorer outcome. The minority of the AS group who no longer met criteria for a full diagnosis of an autism spectrum disorder were



usually free of current psychiatric comorbidity. The high rate of psychiatric/neurodevelopmental comorbidities underscores the need for a full psychiatric/neurodevelopmental assessment at follow-up of males with AS.

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J Child Psychol Psychiatry. 2016 Mar;57:350-52.

**COMMENTARY: TRANSDIAGNOSTIC NEUROSCIENCE OF CHILD AND ADOLESCENT MENTAL DISORDERS-- DIFFERENTIATING DECISION-MAKING IN ATTENTION-DEFICIT/HYPERACTIVITY DISORDER, CONDUCT DISORDER, DEPRESSION AND ANXIETY. A COMMENTARY ON SONUGA-BARKE ET AL. (2016).**

**Rohde LA.**

Sonuga-Barke, Cortese, Fairchild, and Stringaris offer us new insights not only on the neuropsychological processes and neurobiological mechanisms involved in the decision-making process but also how some of the most relevant child mental disorders might impact this process through a very comprehensive review of the pertinent literature. Although it is difficult to select specific points for discussing in a so dense review, I would like to highlight some aspects for 'whetting readers appetite' and seduce them to be in contact with the fascinating neurobiology behind an essential aspect of our lives.

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J Child Psychol Psychiatry. 2016 Feb;57:113-15.

**CHICKENS AND EGGS-HOW SHOULD WE INTERPRET ENVIRONMENT-BEHAVIOR ASSOCIATIONS?**

**Burt SA.**

As usual, the research published in this issue of the Journal of Child Psychology and Psychiatry contains impressive state-of-the-science studies of child and adolescent psychopathology and related issues. Breeman and colleagues, for example, found that children born before 32 weeks gestation or with a very low birth weight (<1,500 g) were not only more frequently diagnosed with Attention-Deficit Hyperactivity Disorder (ADHD) during childhood, but continued to have an increased risk for attention problems up through early adulthood.

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J Neurosurg Pediatr. 2016 Apr;17:491-96.

**PREDICTORS OF DELAYED RECOVERY FOLLOWING PEDIATRIC SPORTS-RELATED CONCUSSION: A CASE-CONTROL STUDY.**

**Miller JH, Gill C, Kuhn EN, et al.**

**OBJECT** Pediatric sports-related concussions are a growing public health concern. The factors that determine injury severity and time to recovery following these concussions are poorly understood. Previous studies suggest that initial symptom severity and diagnosis of attention deficit hyperactivity disorder (ADHD) are predictors of prolonged recovery (> 28 days) after pediatric sports-related concussions. Further analysis of baseline patient characteristics may allow for a more accurate prediction of which patients are at risk for delayed recovery after a sports-related concussion.

**METHODS** The authors performed a single-center retrospective case-control study involving patients cared for at the multidisciplinary Concussion Clinic at Children's of Alabama between August 2011 and January 2013. Patient demographic data, medical history, sport concussion assessment tool 2 (SCAT2) and symptom severity scores, injury characteristics, and patient balance assessments were analyzed for each outcome group. The control group consisted of patients whose symptoms resolved within 28 days. The case group included patients whose symptoms persisted for more than 28 days. The presence or absence of the SCAT2 assessment had a modifying effect on the risk for delayed recovery; therefore, stratum-specific analyses were conducted for patients with recorded SCAT2 scores and for patients without SCAT2 scores. Unadjusted ORs and adjusted ORs (aORs) for an association of delayed recovery outcome with specific risk factors were calculated with logistic regression analysis.

**RESULTS** A total of 294 patients met the inclusion criteria of the study. The case and control groups did not statistically significantly differ in age ( $p = 0.7$ ). For the patients who had received SCAT2 assessments, a

previous history of concussion (aOR 3.67, 95% CI 1.51-8.95), presenting SCAT2 score < 80 (aOR 5.58, 95% CI 2.61-11.93), and female sex (aOR 3.48, 95% CI 1.43-8.49) were all associated with a higher risk for postconcussive symptoms lasting more than 28 days. For patients without SCAT2 scores, female sex and reporting a history of ADHD significantly increased the odds of prolonged recovery (aOR 4.41, 95% CI 1.93-10.07 and aOR 3.87, 95% CI 1.13-13.24, respectively). Concussions resulting from playing a nonhelmet sport were also associated with a higher risk for prolonged symptoms in patients with and without SCAT2 scores (OR 2.59, 95% CI 1.28-5.26 and OR 2.17, 95% CI 0.99-7.73, respectively). Amnesia, balance abnormalities, and a history of migraines were not associated with symptoms lasting longer than 28 days.

**CONCLUSIONS** This case-control study suggests candidate risk factors for predicting prolonged recovery following sports-related concussion. Large prospective cohort studies of youth athletes examined and treated with standardized protocols will be needed to definitively establish these associations and confirm which children are at highest risk for delayed recovery.

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J Pediatr. 2016 Apr;171:20-24.

**TECHNOLOGY AT THE SERVICE OF PEDIATRIC MENTAL HEALTH: REVIEW AND ASSESSMENT.**  
**Aboujaoude E, Salame W.**

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J Pediatr. 2016 Mar;170:97-104.

**NEONATAL INFECTION AND LATER NEURODEVELOPMENTAL RISK IN THE VERY PRETERM INFANT.**  
**Rand KM, Austin NC, Inder TE, et al.**

**OBJECTIVES:** To document associations between confirmed and suspected neonatal infection and motor, cognitive, educational, and mental health outcomes of very preterm (VPT)-born children at 9 years of age; to examine the potential intervening role of cerebral white matter abnormalities (WMAs) and structural development on term magnetic resonance imaging.

**STUDY DESIGN:** A regional cohort of 110 infants born VPT in Christchurch, New Zealand were studied from birth to age of 9 years. Confirmed infection was defined as positive blood, cerebrospinal fluid or urine culture, and/or necrotizing enterocolitis  $\geq$  stage 2. Suspected infection was defined as  $\geq$  5 days of antibiotics with evidence of clinical correlates. At term gestational equivalence, infants underwent structural magnetic resonance imaging. At age 9 years, neuromotor function, IQ, educational achievement, and mental health were assessed.

**RESULTS:** During hospitalization, 25% of VPT infants had confirmed and 23% had suspected infection. Longer-term neurodevelopmental impairments were largely confined to infants with confirmed infection (relative risk 1.4-3.1, vs uninfected). After accounting for other neonatal factors, these infants were at increased risk of severe motor impairment (OR 3.3, 95% CI 1.3-8), attention deficit hyperactivity disorder (ADHD) (OR 3.6, 95% CI 1.6-8), and IQ delay (OR 2.0, 95% CI 1-3.9). Cerebral WMAs contributed to associations between confirmed infection and motor and IQ impairments but not to ADHD ( $P = .005$ ).

**CONCLUSIONS:** Confirmed neonatal infection heightens VPT infants' risk for neurodevelopmental impairment. WMA appears to be an important intervening factor linking infection and severe motor and IQ impairments. Further analysis of the neurologic mechanism accounting for ADHD in infants with infection is needed.

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J Postgrad Med. 2016 Jan;62:12-19.

**IS ANXIETY MORE COMMON IN SCHOOL STUDENTS WITH NEWLY DIAGNOSED SPECIFIC LEARNING DISABILITIES? A CROSS-SECTIONAL QUESTIONNAIRE-BASED STUDY IN MUMBAI, MAHARASHTRA, INDIA.**  
**Thakkar AN, Karande S, Bala N, et al.**

**BACKGROUND AND OBJECTIVES:** School students with specific learning disabilities (SpLDs) experience chronic academic underachievement and resultant stress. The present study aimed to determine if school students with newly diagnosed SpLD were more likely to have anxiety than their regular peers.

**MATERIALS AND METHODS:** The study cases (aged 8-15 years) were recruited from our institute's learning disability clinic. The matched controls were recruited from four schools in Mumbai, Maharashtra, India. Anxiety was measured using the Spence Children's Anxiety Scale (SCAS)-child self-report version questionnaire. Median SCAS scores and the proportion of students with an SCAS score in the "clinical anxiety" range were compared between the groups.

**RESULTS:** SCAS scores were significantly higher in 8-11-year-old learning-disabled male and female students ( $P < 0.0001$  for both groups) and 12-15-year-old female students ( $P = 0.004$ ), as compared with matched controls. A significantly higher number of learning-disabled students were found to have "clinical anxiety" [24.64% vs. 4.35%, crude odds ratio (OR) = 7.19, 95% confidence interval (CI) 2.91-17.78,  $P = 0.0001$ ], as compared with the controls regardless of gender, age group, presence of comorbid attention-deficit/hyperactivity disorder (ADHD), or associated medical conditions. A significantly higher proportion of 8-11-year-old learning-disabled students, especially males, were found to have "clinical anxiety" as compared with 12-15-year-old learning-disabled students (crude OR = 4.38, 95% CI 1.94-9.92,  $P = 0.0004$ ). Gender, presence of comorbid ADHD or associated medical conditions, and type of school attended or curriculum did not impact the prevalence of "clinical anxiety" in learning-disabled students.

**INTERPRETATION AND CONCLUSIONS:** Students with newly diagnosed SpLD have greater odds of being "clinically anxious" relative to their regular peers. We recommend screening for anxiety in children with SpLD immediately after diagnosis so that their optimum rehabilitation can be facilitated.

JAMA Psychiatry. 2016 Jan;73:64-72.

**CORTICAL AND SUBCORTICAL GRAY MATTER VOLUME IN YOUTHS WITH CONDUCT PROBLEMS: A META-ANALYSIS.**  
*Rogers JC, De Brito SA.*

**IMPORTANCE:** A large number of structural neuroimaging studies have used voxel-based morphometry (VBM) to identify gray matter abnormalities in youths with conduct problems (CP), but the findings have been disparate and few have been replicated.

**OBJECTIVE:** To conduct a meta-analysis of published whole-brain structural neuroimaging studies on youths with CP that used VBM methods to facilitate replication and aid further analyses by researchers.

**DATA SOURCES:** The PubMed, ScienceDirect, Scopus, Google Scholar, and Web of Science databases were searched for VBM studies published from January 1, 2007, through March 31, 2015. Manual searches were conducted using title and citation information. Authors were contacted for additional data.

**STUDY SELECTION:** A literature search identified 28 studies. Studies were excluded if they (1) failed to use VBM, (2) failed to report a voxelwise comparison between youths with CP and typically developing (TD) youths, (3) used different significance or extent thresholds throughout the brain, (4) included duplicated datasets, and (5) did not provide peak coordinates or parametric maps after contact with the authors. Thirteen studies were deemed eligible for inclusion (394 youths with CP and 350 TD youths).

**DATA EXTRACTION AND SYNTHESIS:** Anisotropic effect-size signed differential mapping (SDM) was used for voxel-based meta-analyses. Statistical parametric maps comparing gray matter differences between youths with CP and TD youths were available for 11 of the studies, with peak coordinates available for the remaining studies.

**MAIN OUTCOMES AND MEASURES:** Regional gray matter volume (GMV) differences in youths with CP compared with TD youths.

**RESULTS:** Youths with CP had decreased GMV in the left amygdala (SDM estimate = -0.218;  $P < .001$ ) (extending into anterior insula), right insula (SDM estimate = -0.174;  $P < .001$ ) (extending ventrolaterally into the prefrontal cortex and inferiorly into the superior temporal gyrus), left medial superior frontal gyrus (SDM estimate = -0.163;  $P = .001$ ) (extending into the right anterior cingulate cortex), and left fusiform gyrus (SDM estimate = -0.146;  $P = .003$ ). Subgroup meta-analysis assessing age-at-onset effects identified reduced GMV in the left anterior insula (SDM estimate = -0.232;  $P < .001$ ) (extending into amygdala). Meta-regression analyses revealed that greater scores on measures of callous-unemotional traits were associated with a lower reduction in GMV in the left putamen (SDM estimate = -0.911;  $P < .001$ ). The proportion of male and

female youths in the sample was associated with decreased GMV in the left amygdala (SDM estimate = -0.31;  $P < .001$ ) and increased GMV in the right inferior temporal cortex (SDM estimate = 0.755;  $P < .001$ ). While there was no association with comorbid attention-deficit/hyperactivity disorder or IQ, age range was associated with gray matter differences in the left amygdala.

**CONCLUSIONS AND RELEVANCE:** We identified gray matter reductions within the insula, amygdala, frontal and temporal regions in youths with CP as well as inconsistencies in sample characteristics across studies that should be addressed in future research.

J Abnorm Child Psychol. 2016 Aug;44:1217-29.

**FINANCIAL DEPENDENCE OF YOUNG ADULTS WITH CHILDHOOD ADHD.**

**Altszuler AR, Page TF, Gnagy EM, et al.**

This study used data from the Pittsburgh ADHD Longitudinal Study (PALS) to evaluate financial outcomes of young adults (YA) with ADHD relative to comparisons. Participants for this study included 309 individuals who had been diagnosed with ADHD (DSM-III-R or DSM-IV) in childhood and 208 comparison YA without childhood ADHD diagnoses (total  $N = 517$ ) who were followed through age 25. Participants were predominately male (88 %) and Caucasian (84 %). Diagnostic interviews were conducted in childhood. Young adults and their parents reported on financial outcomes and a number of predictor variables. Young adults with ADHD experienced greater financial dependence on family members ( $p < 0.05$ ) and the welfare system ( $p < 0.01$ ) and had lower earnings ( $p < 0.05$ ) than comparisons. ADHD diagnostic status, education attainment, and delinquency were significant predictors of financial outcomes. A projection of lifetime earnings indicated that ADHD group participants could expect to earn \$543,000–\$616,000 less over their lifetimes than comparisons. Due to the propensity of individuals with ADHD to underreport problems, the data are likely to be underestimates. These findings support the need for interventions to improve labor market outcomes as well as the development of interventions that target the management of personal finances for individuals with ADHD in young adulthood.

J Atten Disord. 2016 Aug;20:674-83.

**DIFFERENTIATING BEHAVIORAL RATINGS OF INATTENTION, IMPULSIVITY, AND HYPERACTIVITY IN CHILDREN: EFFECTS ON READING ACHIEVEMENT.**

**Pham AV.**

**Objective:** The purpose of the study is to differentiate between behaviors of ADHD: inattention, hyperactivity, and impulsivity and how each domain contributes to reading achievement in elementary school-aged children.

**Method:** Data from 131 children were collected, which include performance from reading fluency and comprehension measures as well as parent and teacher ratings of ADHD behaviors based on the Diagnostic and Statistical Manual of Mental Disorders (4th ed.; DSM-IV) criteria.

**Results:** Correlation and regression analyses revealed that inattentive behaviors were strongly linked to reading fluency and comprehension. Hyperactivity and impulsive behaviors did not predict reading achievement. A significant two-way interaction was found only for gender and inattention with reading comprehension as the outcome.

**Conclusion:** Many of the behaviors related to inattention strongly predicted reading fluency, reading comprehension, and overall reading ability. Boys who exhibited inattentive behaviors performed more poorly on reading comprehension measures than girls with inattentive behaviors.

J Atten Disord. 2016 Aug;20:647-52.

**MALNUTRITION AND OBESITY IN CHILDREN WITH ADHD.**

**Güngör S, Celiloglu ÖS, Raif SG, et al.**

**Objective:** Low threshold of dissatisfaction and frustration in child and adolescent patients with ADHD lead to changes in dietary pattern with contribution to the development of obesity and other nutritional disorders.

**Methods:** A total of 362 patients with the diagnosis of ADHD and 390 children without any chronic disease were included to the study. We evaluated the anthropometric measurements for all cases.

**Results:** The overweight/obese cases according to weight for height (WFH) and body mass index scores were more likely in ADHD cases than control group. Malnourished cases according to WFH were more common in ADHD cases. Patients with weight standard deviation scores between  $<-2$  and  $>2$  were significantly higher in ADHD cases than the control group patients.

**Conclusion:** Frequency of malnutrition and overweight/obese patients was found higher in ADHD cases compared with control group, and this situation suggested that ADHD is a risk factor for the development of eating disorders.

J Atten Disord. 2016 Aug;20:665-73.

**AGREEMENT AMONG CATEGORICAL, DIMENSIONAL, AND IMPAIRMENT CRITERIA FOR ADHD AND COMMON COMORBIDITIES.**

**Sprafkin J, Steinberg EA, Gadow KD, et al.**

**Objective:** To compare the results of categorically based versus dimensionally based scoring algorithms for a Diagnostic and Statistical Manual of Mental Disorders (4th ed.; DSM-IV)–referenced teacher rating scale for assessing ADHD and commonly co-occurring conditions and to determine their relative agreement with ratings of symptom-induced impairment.

**Method:** Teachers completed Child and Adolescent Symptom Inventory–4R (CASI-4R) ratings for 1,092 youth (ages 6-18 years) referred to a child and adolescent psychiatry outpatient service. Caseness was determined according to DSM-IV symptom count (categorical model) and T-score (dimensional model) criteria.

**Results:** Agreement between symptom count and T-score cutoffs was generally good ( $\kappa = 0.61$ ) for ADHD-Inattentive, ADHD-Hyperactive-Impulsive, ADHD-Combined (except adolescent females), Oppositional Defiant Disorder, and Conduct Disorder, but this was not the case for anxiety and depressive disorders where only 15% of kappas were good. Agreement of impairment cutoff with T-score and symptom count cutoffs ranged from poor to good.

**Conclusion:** In general, although in many cases CASI-4R categorical and dimensional scoring algorithms generated similar results, there was considerable variability across disorders, age groups, scoring method, and in some cases, gender. Moreover, symptom counts and T-scores are not a proxy for assessing impairment suggesting that each scoring strategy likely provides unique information for clinical decision-making.

J Autism Dev Disord. 2016;1-11.

**RELATIONSHIP BETWEEN EXECUTIVE FUNCTIONING AND SYMPTOMS OF ATTENTION-DEFICIT/HYPERACTIVITY DISORDER AND AUTISM SPECTRUM DISORDER IN 6-8 YEAR OLD CHILDREN.**

**Neely RJ, Green JL, Sciberras E, et al.**

This study examined relationships between executive functioning (EF) and ADHD/ASD symptoms in 339 6–8 year-old children to characterise EF profiles associated with ADHD and ADHD + ASD. ADHD status was assessed using screening surveys and diagnostic interviews. ASD symptoms were measured using the Social Communication Questionnaire, and children completed assessments of EF. We found the EF profile of children with ADHD + ASD did not differ from ADHD-alone and that lower-order cognitive skills contributed significantly to EF. Dimensionally, ASD and inattention symptoms were differentially associated with EF, whereas hyperactivity symptoms were unrelated to EF. Differences between categorical and dimensional



findings suggest it is important to use both diagnostic and symptom based approaches in clinical settings when assessing these children's functional abilities.

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J Child Neurol. 2016;31:1245-49.

**COLOR VISION DEFICIENCY AND FUNCTIONAL DISORDERS AMONG ISRAELI MALE ADOLESCENTS BETWEEN 2007 AND 2013.**

**Berger A, Findler M, Maymon D, et al.**

Color vision deficiency has been associated with educational difficulties among male children, as well as attention-deficit hyperactivity disorder (ADHD). We examined the association of color vision deficiency with functional conditions, including ADHD, irritable bowel syndrome, enuresis and somatoform disorders, in a large population of male adolescents. We included all Israeli male adolescents that underwent medical and cognitive examinations during conscription between the years 2007 and 2013. The prevalence of ADHD, irritable bowel syndrome, enuresis, and somatoform disorders among color vision deficiency patients was compared to a control group. The study included 305 964 males aging 17 - 0.6, of which 7584 (2.5%) had color vision deficiency. Using a multivariable analysis, the probability for irritable bowel syndrome, enuresis, and somatoform disorders among color vision deficiency patients was increased by 1.41, 1.94, and 3.87, respectively ( $P < .05$ ). No significant association was found between ADHD and color vision deficiency. Color vision abnormalities are associated with functional disorders in male adolescents, including irritable bowel syndrome, enuresis, and somatoform disorders.

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J Child Neurol. 2016 Jul;31:957-64.

**GUANFACINE USE IN CHILDREN WITH DOWN SYNDROME AND COMORBID ATTENTION-DEFICIT HYPERACTIVITY DISORDER (ADHD) WITH DISRUPTIVE BEHAVIORS.**

**Capone GT, Brecher L, Bay M.**

The purpose of this study was to characterize children with Down syndrome and attention-deficit hyperactivity disorder (ADHD) with disruptive behaviors using the Aberrant Behavior Checklist (ABC), and to measure the treatment effects of guanfacine on maladaptive behaviors. Subjects were enrolled from a group of outpatients who visited our clinic between 2002 and 2007. Subjects ( $N = 23$ ) were children with Down syndrome ages 4 to 12 years (mean  $7.4 \pm 4.1$ ), who met criteria for ADHD according to the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition. The Aberrant Behavior Checklist Irritability and Hyperactivity subscales each showed a significant decrease ( $P < .0001$ ) at follow-up. The mean decline on Hyperactivity was 25% ( $-7.8$  points), and for Irritability, 25% ( $-3.5$  points). The mean composite score also declined by 24% ( $-12$  points). Effect size differences on Irritability were moderate, whereas differences on Hyperactivity and composite score appeared large. Clinically important target behaviors were reduced. Medication was generally well tolerated and the incidence of treatment emergent side effects remained low.

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J Child Neurol. 2016;31:1250-56.

**THE DOPAMINE RECEPTOR D5 MAY INFLUENCE AGE OF ONSET: AN EXPLORATORY STUDY ON INDO-CAUCASOID ADHD SUBJECTS.**

**Maitra S, Sarkar K, Sinha S, et al.**

The objective was to investigate contribution of the dopamine receptor 5 (DRD5) gene variants in the symptoms of attention-deficit/hyperactivity disorder (ADHD) probands since brain regions identified to be affected in these group of patients have higher expression of the DRD5 receptor. Out of 22 exonic variants, 19 were monomorphic in the Indo-Caucasoid individuals. rs6283 "C" and rs113828117 "A" exhibited significant higher occurrence in families with ADHD probands. Several haplotypes showed biased occurrence in the probands. Early and late onset groups exhibited significantly different genotypic frequencies. A new G>A substitution was observed in the control samples only. The late onset group

exhibited higher scores for hyperactivity as compared to the early onset group. The authors infer that the age of onset of ADHD may at least partially be affected by DRD5 variants warranting further investigation on the role of DRD5 in the disease etiology.

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J Child Psychol Psychiatry. 2016 Aug;57:967-75.

**ASSOCIATION BETWEEN IMMIGRANT BACKGROUND AND ADHD: A NATIONWIDE POPULATION-BASED CASE-CONTROL STUDY.**

**Lehti V, Chudal R, Suominen A, et al.**

**Background:** Information about psychiatric disorders among those with immigrant parents is important for early detection and service development. The aim of this study is to examine the association between parental immigration and the diagnosis of attention-deficit hyperactivity disorder (ADHD) in offspring in Finland.

**Methods:** This matched case-control study was based on a national birth cohort. The sample included all singletons who were born in Finland in 1991–2005 and diagnosed with ADHD by the year 2011 ( $n = 10,409$ ) and their matched controls ( $n = 39,124$ ). Nationwide registers were used to identify participants and to gather information on the parents' country of birth and native language. Conditional logistic regression analyses were conducted using maternal and paternal migration status and region of birth as well as time since maternal migration as exposure factors.

**Results:** The likelihood of being diagnosed with ADHD was significantly increased among children of two immigrant parents [adjusted odds ratio (aOR) 4.7, 95% CI 3.4–6.6] and children of an immigrant father (aOR 1.9, 95% CI 1.6–2.2). The likelihood of receiving an ADHD diagnosis was equal among children whose mother was a recent immigrant when she gave birth and those whose mother had stayed in Finland at least for a year before birth. The association between parental migration and ADHD diagnosis was strongest among fathers born in sub-Saharan Africa or Latin America and among mothers born in sub-Saharan Africa or North Africa and Middle East. Children, whose parents were born in countries with low Human Development Index (HDI), were more often diagnosed with ADHD.

**Conclusions:** The increased likelihood of ADHD diagnosis among children of immigrants indicates increased exposure to environmental risk factors, differences in the use of health services, or challenges in diagnosing immigrants' children.

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J Child Psychol Psychiatry. 2016 Aug;57:947-56.

**BEHAVIORAL SENSITIVITY TO CHANGING REINFORCEMENT CONTINGENCIES IN ATTENTION-DEFICIT HYPERACTIVITY DISORDER.**

**Alsop B, Furukawa E, Sowerby P, et al.**

**Background:** Altered sensitivity to positive reinforcement has been hypothesized to contribute to the symptoms of attention-deficit hyperactivity disorder (ADHD). In this study, we evaluated the ability of children with and without ADHD to adapt their behavior to changing reinforcer availability.

**Method:** Of one hundred sixty-seven children, 97 diagnosed with ADHD completed a signal-detection task in which correct discriminations between two stimuli were associated with different frequencies of reinforcement. The response alternative associated with the higher rate of reinforcement switched twice during the task without warning. For a subset of participants, this was followed by trials for which no reinforcement was delivered, irrespective of performance.

**Results:** Children in both groups developed an initial bias toward the more frequently reinforced response alternative. When the response alternative associated with the higher rate of reinforcement switched, the children's response allocation (bias) followed suit, but this effect was significantly smaller for children with ADHD. When reinforcement was discontinued, only children in the control group modified their response pattern.

**Conclusions:** Children with ADHD adjust their behavioral responses to changing reinforcer availability less than typically developing children, when reinforcement is intermittent and the association between an action

and its consequences is uncertain. This may explain the difficulty children with ADHD have adapting their behavior to new situations, with different reinforcement contingencies, in daily life.

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J Consult Clin Psychol. 2016;84:699-712.

**PARENT-TEEN BEHAVIOR THERAPY + MOTIVATIONAL INTERVIEWING FOR ADOLESCENTS WITH ADHD.**

**Sibley MH, Graziano PA, Kuriyan AB, et al.**

**Objective:** This study evaluates a parent-teen skills-based therapy for attention deficit/hyperactivity disorder (ADHD) blended with motivational interviewing (MI) to enhance family engagement. Supporting Teens' Autonomy Daily (STAND) is an adolescent-specific treatment for ADHD that targets empirically identified adolescent (i.e., organization, time management, and planning, or OTP skills) and parent-based (i.e., monitoring and contingency management) mechanisms of long-term outcome through individual parent-teen sessions.

**Method:** The current randomized trial (N = 128) evaluates efficacy at post treatment and 6-month follow-up. Participants were ethnically diverse teens (7.7% non-Hispanic White, 10.8% African American, 78.5% Hispanic, 3.0% other) randomly assigned to STAND or Treatment As Usual (TAU).

**Results:** Primary findings were that (1) STAND was delivered in an MI-adherent fashion and most families fully engaged in treatment (85% completed); (2) STAND produced a range of significant acute effects on ADHD symptoms, OTP skills, homework behavior, parent-teen contracting, implementation of home privileges, parenting stress, and daily homework recording; and (3) 6 months after treatment ceased, effects on ADHD symptom severity, OTP skills, and parenting stress maintained, while parent use of contracting and privilege implementation strategies, as well as teen daily homework recording and homework behavior gains, were not maintained.

**Conclusion:** Skills-based behavior therapy blended with MI is an acutely efficacious treatment for adolescents with ADHD although more work is needed to establish the nature of long-term effects.

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J Dev Behav Pediatr. 2016 Jul;37:511-13.

**ATTENTION-DEFICIT/HYPERACTIVITY DISORDER–RELATED IMPULSIVITY AND CYBERBULLYING IN SOCIAL MEDIA.**

**Reilly M, Fogler J, Selkie E, et al.**

**Case:** Sarah is a 13-year-old eighth grader who was recently diagnosed for the first time with attention-deficit/hyperactivity disorder (ADHD)-inattentive type, and the family elected to treat her with behavioral interventions to help her organization and attention. She had struggled with distractibility and disorganization since the fourth grade. At home, Sarah's mother described her as 'spacey' and unable to complete the morning routine without constant supervision. Over time, her mother observed that it seemed as if Sarah had given up on school. As Sarah became an adolescent, her self-esteem suffered because of her academic struggles, and she placed increasing emphasis on her appearance, including focus on remaining thin and refusing to leave the house without makeup. It was in this context that Sarah recently posted photographs of herself in various stages of undress and/or drinking alcohol on Snapchat, a photograph-sharing application in which users can send 'snaps'—photographs that disappear soon after opening. However, snap recipients can take a screenshot or photograph of the snap, thereby saving the image. For unknown reasons, Sarah's close female friend took screenshots of these provocative photographs and sent them to their classmates and Sarah's older brother. Sarah's family contacted the police and has been working with her school to address this incident. This experience resulted in significant family stress and distrust of Sarah. For example, her mother took away her cell phone and laptop and has 'grounded her' for a month from all out of school activities. Sarah's family seeks guidance regarding teaching Sarah about using social media responsibly and preventing this from happening again. Sarah's mom comes to your urgent care session asking for help because she does not feel that Sarah has 'learned her lesson.' What would you do next?

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J Dev Behav Pediatr. 2016 Jul;37:491-95.

**TREATMENT EFFICACY OF COMBINED SERTRALINE AND GUANFACINE IN COMORBID OBSESSIVE–COMPULSIVE DISORDER AND ATTENTION DEFICIT/HYPERACTIVITY DISORDER: TWO CASE STUDIES.**

**Taormina SP, Galloway MP, Rosenberg DR.**

**Objective:** Treatment of obsessive–compulsive disorder (OCD) is complicated by comorbid psychiatric disorders. Successful treatment of 2 pediatric patients with severe OCD and comorbid attention deficit/hyperactivity disorder (ADHD) is described.

**Method:** A report on 2 pediatric clinical cases (Ages 9 and 10) with comorbid OCD and ADHD was used to describe response to medication management through the serotonin transporter inhibitor, sertraline, and the noradrenergic  $\alpha$ 2A receptor agonist, guanfacine, along with cognitive behavioral therapy.

**Results:** Cognitive behavioral therapy combined with titrated doses of the serotonin transporter inhibitor, sertraline, and the noradrenergic  $\alpha$ 2A receptor agonist, guanfacine resolved OCD symptoms and the underlying ADHD.

**Conclusion:** The novel observations support a focused psychological and pharmacological approach to successful treatment of complex symptoms in patients with comorbid OCD and ADHD. Limitations to generalizability are discussed.

J Environ Public Health. 2016;2016.

**CROSS-SECTIONAL STUDY OF POLYBROMINATED FLAME RETARDANTS AND SELF-REPORTED ATTENTION DEFICIT HYPERACTIVITY DISORDER IN US YOUTH AGED 12-15 (NHANES 2003-2004) .**

**Przybyla J, Kile ML, Smit E, et al.**

**Background.** Animal toxicity tests and epidemiological studies suggest that exposure to PBDEs can alter attention behavior, yet few studies have examined their association with diagnosis of attention deficit hyperactivity disorder (ADHD) in adolescents.

**Methods.** Logistic regression was used to examine the cross-sectional association between ADHD and lipid and non-lipid adjusted blood serum concentrations of 2',4-tribromodiphenyl ether (BDE-28), 2,2',4,4'-tetrabromodiphenylether (BDE-47), 2,2',4,4',5-pentabromodiphenyl ether (BDE-99), 2,2',4,4',5,5'-pentabromodiphenyl ether (BDE-100), 2,2',4,4',5,5'-hexabromodiphenyl ether (BDE-153), serum PBDEs, above/below the 75th percentile of serum PBDEs, and tertiles of serum PBDE in 12-15-year-olds (N = 292) using the National Health and Nutrition Examination Survey (NHANES) 2003-2004.

**Results.** The ADHD weighted prevalence was 13.57%. The weighted adjusted odds ratios (AOR) and 95% confidence interval (CI) between ADHD diagnosis and lipid adjusted BDE-28, BDE-47, BDE-99, BDE-100, BDE-153, serum total PBDE, serum PBDE concentrations above the 75th percentile, and serum PBDE concentrations in the second or third tertile were 1.16 (95% CI: 0.51, 2.67), 1.36 (95% CI: 0.72, 2.56), 1.51 (95% CI: 0.70, 3.25), 1.53 (95% CI: 0.73, 3.23), 1.43 (95% CI: 0.57, 3.56), 1.41 (0.71, 2.83), 0.59 (0.10, 3.56), 6.16 (1.19, 31.90), and 0.99 (0.23, 4.29).

**Conclusions.** We observed no association between serum PBDE concentrations and ADHD in US youths.

J Intellect Disabil Res. 2016;60:790.

**TIME DISCRIMINATION IN CHILDREN WITH ASD, ADHD, AND CO-MORBID ASD+ADHD.**

**Jiamjaroenkul J, Tye C, Ashwood K, et al.**

**Aim:** Overlaps between autism spectrum disorder (ASD) and attention deficit hyperactivity disorder (ADHD) commonly occur. Deficits in cognitive function have been demonstrated in both disorders, yet these impairments have never been directly compared across pure and comorbid groups using time discrimination task. This study investigates and compares time discrimination in children diagnosed with ASD, ADHD, and co-morbid ASD +ADHD.

**Method:** Time discrimination task was administered to boys (7 to 16 years old) with ASD (n=17), ADHD (n=30), co-morbid ASD+ADHD (n=35), and typically developing controls (TD; n=20).

**Results:** Children with ASD, ADHD, co-morbid ASD+ADHD, and TD showed a trend towards significant difference in time discrimination ( $p < 0.1$ ). The deficits in time discrimination were observed in the combined group of ADHD and co-morbid ASD+ADHD ( $p < 0.05$ ). The significant correlations between severity of inattentive symptoms and deficits in time discrimination were also observed in the whole sample.

**Conclusions:** This study is the first study using a four-group design to compare ability in time discrimination. It could be concluded that the deficit in time discrimination is likely pronounced in children with inattentive symptoms.

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J Intellect Disabil Res. 2016;60:674.

**ASSOCIATION BETWEEN AUTISM SYMPTOMS AND CHILD AND FAMILY FUNCTIONING IN CHILDREN WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER: A COMMUNITY-BASED STUDY.**

**Green J.**

**Aim:** This study examined the association between autism symptoms and child and family functioning in children with attention deficit hyperactivity disorder (ADHD).

**Method:** 164 children (6 to 10 year olds) attending 43 schools in Melbourne, Australia, who were participating in a longitudinal cohort study, were included. ADHD cases were ascertained using screening and confirmation from a diagnostic interview. Autism symptoms were identified using the Social Communication Questionnaire. A range of child and family outcome measures were used.

**Results:** 23% of children with ADHD had clinically elevated autism symptoms. In adjusted analyses, greater autism symptoms were associated with more peer problems, poorer child and family quality of life (QoL), higher couple conflict, and greater child mental health difficulties. Parents of children with ADHD and clinically elevated symptoms of autism had less self-efficacy and poorer family QoL.

**Conclusions:** Autism symptoms are associated with poorer child and family functioning in children with ADHD. The association between ASD symptoms and poorer family functioning appears to be largely related to co-morbid internalising and externalising symptoms, ADHD severity and socioeconomic status.

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J Intellect Disabil Res. 2016;60:632.

**EARLY CHILDHOOD BEHAVIOUR DISORDERS AND MOTHER WELLBEING: PREDICTING TO A DECADE LATER.**

**Baker B, Blacher J.**

**Aim:** To study the trajectory of behaviour disorders in children with intellectual disabilities (ID) or typical cognitive development. Do behaviour disorders and mother distress at child age three years predict behaviour disorders a decade later?

**Method:** We studied 114 children with or without ID longitudinally; this report is based on age 3 and age 13 assessments. The outcome was behaviour disorders in adolescence, assessed with Child Behavior Checklist (CBCL) scales: total behaviour problems, ADHD, and anxiety disorders. Predictors included the child behaviour problems at age 3, as both continuous and binary (clinical range vs. not) variables and the mothers' stress and psychological adjustment, assessed by the Family Impact Questionnaire (Negative Impact scale) and the Symptom Checklist 36.

**Results:** CBCL scores at age 3 were highly predictive of CBCL scores a decade later, for children with or without ID. Moreover, mothers' stress and psychological problems at child age 3 accounted for significant variance in youth CBCL scores a decade later.

**Conclusions:** These findings underscore the importance of interventions in early childhood to reduce child behaviour problems and/or to help mothers cope better with stress.

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J Neural Transm. 2016;123:991-1000.

**THE AETIOLOGICAL ASSOCIATION BETWEEN THE DYNAMICS OF CORTISOL PRODUCTIVITY AND ADHD.**

**Pinto R, Rijdsdijk F, Ouellet-Morin I, et al.**

Attention-deficit/hyperactivity disorder (ADHD) has been linked to dysregulation of the hypothalamic-pituitary-adrenal (HPA) axis, indexed by salivary cortisol. The phenotypic and aetiological association of cortisol productivity with ADHD was investigated. A selected twin design using 68 male twin-pairs aged 12-15, concordant or discordant for high ADHD symptom scores, or control twin-pairs with low ADHD symptoms, based on developmentally stable parental ADHD ratings. A genetic growth curve model was applied to cortisol samples obtained across three points during a cognitive-electroencephalography assessment, to examine the aetiological overlap of ADHD affection status (high versus low ADHD symptom scores) with latent intercept and slope factors. A significant phenotypic correlation emerged between ADHD and the slope factor, with cortisol levels dropping faster for the group with high ADHD symptom scores. The analyses further suggested this overlap was mostly driven by correlated genetic effects. We identified change in cortisol activity over time as significantly associated with ADHD affection status, primarily explained by shared genetic effects, suggesting that blunted cortisol productivity can be a marker of genetic risk in ADHD.

Journal of Pediatric Neurosciences. 2016;11:137-39.

**PSYCHIATRIC MANIFESTATIONS OF CONGENITAL RUBELLA SYNDROME: A CASE REPORT AND REVIEW OF LITERATURE.**

**Chauhan N, Sen M, Jhanda S, et al.**

Neurodevelopmental disorders are known to have varied etiology. Among known etiologic causes, congenital rubella syndrome (CRS) is reported to be one of the infections associated with neurodevelopmental disorders. CRS has been reported to be associated with large number of psychiatric manifestation. However, data from developing countries on psychiatric manifestations of CRS are nonexistent. In this report, we present the case of a 7-year-old boy, who presented with mental retardation, atypical autism, and attention deficit hyperactivity disorder. Since birth, the child was found to have congenital cardiac defects and was found to have bilateral profound sensorineural hearing loss since the age of 6 months. Magnetic resonance imaging showed multifocal symmetrical T2/fluid attenuated inversion recovery hyperintensities in bilateral cerebral hemisphere suggestive of sequelae of congenital rubella infection.

Journal of Pharmaceutical Sciences and Research. 2016;8:613-15.

**DENTAL CARIES AND CHILDREN WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER (ADHD) □ A REVIEW.**

**Manoharan S, Krishnamoorthy K.**

**Aim** Dental caries in adolescents with attention deficit hyperactivity disorder-A Review

**Objective** Attention deficit hyperactive disorder (ADHD) adolescents have higher prevalence of caries.

**Background** Attention deficit hyperactivity disorder (ADHD) is a neurodevelopmental psychiatric disorder in which there are significant problems with executive functions (e.g., attentional control and inhibitory control) that cause attention deficits, hyperactivity, or impulsiveness which is not appropriate for a person's age. ADHD is diagnosed approximately three times more in boys than in girls. About 30–50% of people diagnosed in childhood continue to have symptoms into adulthood and between 2–5% of adults have the condition.

**Reason** My cousin being suffering from this disorder, encouraged me to undertake this research.

J Psychiatr Res. 2016;82:141-48.

**ADHD AND EXECUTIVE FUNCTIONING DEFICITS IN OCD YOUTHS WHO HOARD.**

**Park JM, Samuels JF, Grados MA, et al.**

Hoarding is common among youth with obsessive compulsive disorder (OCD), with up to 26% of OCD youth exhibiting hoarding symptoms. Recent evidence from adult hoarding and OCD cohorts suggests that

hoarding symptoms are associated with executive functioning deficits similar to those observed in subjects with attention deficit hyperactivity disorder (ADHD). However, while hoarding behavior often onsets during childhood, there is little information about executive function deficits and ADHD in affected children and adolescents. The study sample included 431 youths (ages 6 to 17 years) diagnosed with OCD who participated in the OCD Collaborative Genetics Study and the OCD Collaborative Genetics Association Study and completed a series of clinician-administered and parent report assessments, including diagnostic interviews and measures of executive functioning (Behavior Rating Inventory of Executive Functioning; BRIEF) and hoarding severity (Hoarding Rating Scale-Interview; HRS-I). 113 youths (26%) had clinically significant levels of hoarding compulsions. Youths with and without hoarding differed significantly on most executive functioning subdomains and composite indices as measured by the parent-rated BRIEF. Groups did not differ in the frequency of full DSM-IV ADHD diagnoses; however, the hoarding group had significantly greater number of inattention and hyperactivity symptoms compared to the non-hoarding group. In multivariate models, we found that overall BRIEF scores were related to hoarding severity, adjusting for age, gender and ADHD symptoms. These findings suggest an association between hoarding and executive functioning deficits in youths with OCD, and assessing executive functioning may be important for investigating the etiology and treatment of children and adolescents with hoarding and OCD.

J Psychiatr Res. 2016;82:91-99.

**SELF-REPORT OF ADHD SHOWS LIMITED AGREEMENT WITH OBJECTIVE MARKERS OF PERSISTENCE AND REMITTANCE.**

**Du Rietz E, Cheung CHM, McLoughlin G, et al.**

**Objective** A controversial issue is whether self-report of symptoms and impairment is sufficient for diagnosis of attention-deficit/hyperactivity disorder (ADHD) in adolescents and adults in the absence of other informants, such as parents. The present study investigated how well self-report is reflected by cognitive-neurophysiological and actigraph measures, which we have previously shown to discriminate between ADHD persisters, remitters and controls using parent-report (Cheung et al., 2015; Brit J Psychiat <http://dx.doi.org/10.1192/bjp.bp.114.145185>).

**Method** Parent- and self-reported ADHD symptoms and impairment, together with cognitive, electroencephalogram (EEG) frequency, event-related potential (ERP) and actigraph measures were obtained from 108 adolescents and young adults with childhood ADHD and 167 controls.

**Results** Participants reported lower levels of ADHD symptoms and impairments than parents ( $p < .05$ ) and the ADHD persistence rate based on self-report was low at 44%, compared to the persistence rate of 79% previously reported based on parent-report. Regression analyses showed that the objective measures distinguished poorly between ADHD persistent and remittent groups based on self-report, in contrast to findings based on parent-report (Cheung et al., 2015), although the measures differentiated well between ADHD persisters and controls. Correlation analyses revealed that self-reported impairment significantly correlated with fewer of the objective measures, despite parent- and self-reported symptoms showing similar correlations with the measures.

**Conclusions** The findings show that self-reported ADHD outcome is not as well reflected by cognitive-neurophysiological and movement correlates as we previously found for parent-reported ADHD.

J Psychiatry Neurosci. 2016;41:272-79.

**VOXEL-BASED MORPHOMETRY ANALYSIS REVEALS FRONTAL BRAIN DIFFERENCES IN PARTICIPANTS WITH ADHD AND THEIR UNAFFECTED SIBLINGS.**

**Bralten J, Greven CU, Franke B, et al.**

**Background:** Data on structural brain alterations in patients with attention-deficit/hyperactivity disorder (ADHD) have been inconsistent. Both ADHD and brain volumes have a strong genetic loading, but whether brain alterations in patients with ADHD are familial has been underexplored. We aimed to detect structural

brain alterations in adolescents and young adults with ADHD compared with healthy controls. We examined whether these alterations were also found in their unaffected siblings, using a uniquely large sample.

**Methods:** We performed voxelbased morphometry analyses on MRI scans of patients with ADHD, their unaffected siblings and typically developing controls. We identified brain areas that differed between participants with ADHD and controls and investigated whether these areas were different in unaffected siblings. Influences of medication use, age, sex and IQ were considered.

**Results:** Our sample included 307 patients with ADHD, 169 unaffected siblings and 196 typically developing controls (mean age 17.2 [range 8–30] yr). Compared with controls, participants with ADHD had significantly smaller grey matter volume in 5 clusters located in the precentral gyrus, medial and orbitofrontal cortex, and (para)cingulate cortices. Unaffected siblings showed intermediate volumes significantly different from controls in 4 of these clusters (all except the precentral gyrus). Medication use, age, sex and IQ did not have an undue influence on the results.

**Limitations:** Our sample was heterogeneous, most participants with ADHD were taking medication, and the comparison was cross-sectional.

**Conclusion:** Brain areas involved in decision making, motivation, cognitive control and motor functioning were smaller in participants with ADHD than in controls. Investigation of unaffected siblings indicated familiarity of 4 of the structural brain differences, supporting their potential in molecular genetic analyses in ADHD research.

J Psychopathol Behav Assess. 2016;1-10.

#### **NEGATIVE HALO EFFECTS IN PARENT RATINGS OF ADHD AND ODD.**

**DeVries LN, Hartung CM, Golden TL.**

Parent ratings of ADHD and ODD symptoms depicted in written vignettes were examined for negative halo effects. Participants were 82 parents of children ages 6–12. Both unidirectional and bidirectional halo effects were found but to a lesser extent than in similar studies with teacher and college student raters. Specifically, parents were more likely to: (a) rate a child as inattentive in the presence of hyperactivity symptoms; (b) more likely to rate a child as oppositional in the presence of inattention and hyperactivity symptoms; and (c) more likely to rate a child as inattentive and hyperactive in the presence of oppositionality symptoms. Several specific symptoms were also found to be particularly susceptible to halo effects. Results suggest that parents may be more discerning raters of disruptive behavior disorders than teachers or college students and less prone to negative halo effects. Implications for clinical practice and future research directions are discussed.

J Psychopathol Behav Assess. 2016;1-13.

#### **SOCIAL SKILLS MEDIATE THE ASSOCIATION OF ADHD AND DEPRESSION IN PREADOLESCENTS.**

**Feldman JS, Tung I, Lee SS.**

Childhood attention-deficit/hyperactivity disorder (ADHD) is a replicated risk factor for depression, but the explanatory factors underlying this association have not been reliably identified. Given that social skills (i.e., cooperation, assertion, responsibility, self-control) are sensitive to early ADHD and predict later depression, we tested whether individual differences in social skills individually and collectively mediated predictions of depressive symptoms from early ADHD symptoms. In an ethnically diverse (50 % non-Caucasian) sample of 232 children with (n = 124) and without ADHD (n = 108) followed prospectively for two years (aged 5–10 at Wave 1; 7–12 at Wave 2), we gathered multi-informant (i.e., parent, teacher) and multi-method (e.g., rating scale, structured interview) assessment of key constructs. Using a multiple mediation framework with bootstrapping and statistical control of sex, Wave 1 depression, Wave 1 oppositional defiant disorder (ODD), Wave 1 anxiety, and Wave 2 ADHD symptoms, an independent mediation effect emerged for parent-rated self-control in the prediction of Wave 2 depression (parent-rated) from Wave 1 ADHD symptoms (combined parent and teacher ratings). Teacher-rated social skills at Wave 1 also collectively mediated this association,

with teacher-rated assertion emerging as a unique mediator. We discuss the role of social skills in emergent depression among youth with ADHD and consider implications for prevention and intervention.

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J Subst Abuse Treat. 2016;70:21-27.

**SMOKING CESSATION AND ADOLESCENT TREATMENT RESPONSE WITH COMORBID ADHD.**

**Pagano ME, Delos-Reyes CM, Wasilow S, et al.**

Minors entering treatment for alcohol and other drug (AOD) use disorders tend to smoke at high rates, and many have comorbid attention deficit hyperactivity disorder (ADHD). Clear-air laws force patients to refrain from smoking on the premises of AOD treatment facilities, which may hinder the progress of treatment-seeking populations who smoke and struggle with ADHD comorbidity in particular. This study explores clinical characteristics associated with smoking among youths presenting for residential treatment, clinical characteristics associated with smoking cessation, and the impact of smoking cessation with ADHD comorbidity on AOD treatment response. Participants were 195 adolescents (52% female, aged 14–18 years) court-referred to residential treatment. Data were collected at intake, prospectively each week for the 10-week treatment period, and at discharge. Two-thirds (67%) of the enrollment sample entered treatment smoking half a pack a day on average, a large proportion (50%) of which did not smoke during treatment. ADHD patients were more likely to smoke before and during treatment except for those who got active in service and step-work. Quitting smoking did not adversely affect AOD outcomes and was associated with better prognosis of lowered AOD cravings for youths with and without ADHD. Smoking cessation during adolescent AOD treatment is recommended with provision of pharmaceutical and/or behavioral modalities that reduce nicotine withdrawal.

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J Am Acad Child Adolesc Psychiatry. 2016 Aug;55:657-66.

**COMBINED STIMULANT AND GUANFACINE ADMINISTRATION IN ATTENTION-DEFICIT/HYPERACTIVITY DISORDER: A CONTROLLED, COMPARATIVE STUDY.**

**McCracken JT, McGough JJ, Loo SK, et al.**

**Objective:** Because models of attention-deficit/hyperactivity disorder (ADHD) therapeutics emphasize benefits of both enhanced dopaminergic and noradrenergic signaling, strategies to enhance D1 and  $\alpha 2A$  agonism may yield enhanced clinical and cognitive responses. This study tested the hypothesis that combined effects of a dopamine and noradrenergic agonist, d-methylphenidate extended-release (DMPH) with guanfacine (GUAN), an  $\alpha 2A$  receptor agonist, would be clinically superior to either monotherapy and would have equal tolerability.

**Method:** An 8-week, double-blind, 3-arm, comparative trial randomized 7- to 14-year-olds with DSM-IV ADHD to GUAN (1-3 mg/day), DMPH (5-20 mg/day), or a combination (COMB) with fixed-flexible dosing. Outcome measures were the ADHD Rating Scale IV (ADHD-RS-IV) and the Clinical Global Impression-Improvement (CGI-I) scale. Data on adverse events and safety measures were obtained.

**Results:** A total of 207 participants were randomized and received drug. Analyses showed significant treatment group main effects for ADHD-RS-IV ADHD total ( $p = .0001$ ) and inattentive symptoms ( $p = .0001$ ). COMB demonstrated small but consistently greater reductions in ADHD-RS-IV Inattentive subscale scores versus monotherapies (DMPH:  $p = .05$ ;  $f^2 = .02$ ; and GUAN:  $p = .02$ ;  $f^2 = .02$ ), and was associated with a greater positive response rate by CGI-I ( $p = .01$ ). No serious cardiovascular events occurred. Sedation, somnolence, lethargy, and fatigue were greater in both guanfacine groups. All treatments were well tolerated.

**Conclusion:** COMB showed consistent evidence of clinical benefits over monotherapies, possibly reflecting advantages of greater combined dopaminergic and  $\alpha 2A$  agonism. Adverse events were generally mild to moderate, and COMB treatment showed no differences in safety or tolerability.

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J Am Acad Child Adolesc Psychiatry. 2016 Aug;55:674-82.

**EFFECTS OF D-METHYLPHENIDATE, GUANFACINE, AND THEIR COMBINATION ON ELECTROENCEPHALOGRAM RESTING STATE SPECTRAL POWER IN ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.**

**Loo SK, Bilder RM, Cho AL, et al.**

**Objective:** Psychostimulant medications are the gold standard of treatment for attention-deficit/hyperactivity disorder (ADHD); however, a significant minority (~30%) of individuals with ADHD fail to respond favorably. Noradrenergic agents are increasingly used as ADHD monotherapies or adjuncts for suboptimal stimulant response, yet knowledge of their cortical effects is limited. This study is the first to examine comparative effects of guanfacine (an adrenergic 2A agonist), psychostimulant, and their combination on resting state cortical activity in ADHD.

**Method:** The sample comprised 179 participants aged 7 to 14 years old with ADHD (113 boys, 55 girls). Participants were randomized to 1 of 3 blinded conditions: guanfacine (GUAN), d-methylphenidate (DMPH), or the combination (COMB). Electroencephalography (EEG) was performed pre-, mid-, and post-medication titration, with concomitant assessment of behavioral and cognitive functioning.

**Results:** Analyses of spectral power measures during resting EEG suggested that each medication condition displayed a distinct profile of effects on cortical activity. Significant time effects suggested that GUAN decreased global alpha band (8-12 hertz [Hz]) power, DMPH and COMB increased centro-parietal beta band (13-21 Hz) power, and COMB resulted in decreased theta band (4-7 Hz) power. Relative to other medication groups, COMB was associated with significantly lower theta band power and DMPH with higher beta band power compared with those in the GUAN group. Medication-related changes in theta power were correlated with improvements in behavioral and cognitive functioning.

**Conclusion:** These data reveal distinct underlying medication-related effects on neural mechanisms. The COMB condition uniquely exhibited an EEG profile that was associated with improved behavioral and cognitive functioning.

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J Am Acad Child Adolesc Psychiatry. 2016 Aug;55:667-73.

**COGNITIVE EFFECTS OF STIMULANT, GUANFACINE, AND COMBINED TREATMENT IN CHILD AND ADOLESCENT ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.**

**Bilder RM, Loo SK, McGough JJ, et al.**

**Objective:** Psychostimulants are partially effective in reducing cognitive dysfunction associated with attention-deficit/hyperactivity disorder (ADHD). Cognitive effects of guanfacine, an alternative treatment, are poorly understood. Given its distinct action on  $\alpha_2A$  receptors, guanfacine may have different or complementary effects relative to stimulants. This study tested stimulant and guanfacine monotherapies relative to combined treatment on cognitive functions important in ADHD.

**Method:** Children with ADHD ( $n = 182$ ; aged 7-14 years) completed an 8-week, double blind, randomized, controlled trial with 3 arms: d-methylphenidate (DMPH), guanfacine (GUAN), or combination treatment with DMPH and GUAN (COMB). A nonclinical comparison group ( $n = 93$ ) had baseline testing, and a subset was retested 8 weeks later ( $n = 38$ ). Analyses examined treatment effects in 4 cognitive domains (working memory, response inhibition, reaction time, and reaction time variability) constructed from 20 variables.

**Results:** The ADHD group showed impaired working memory relative to the nonclinical comparison group (effect size =  $-0.53$  SD unit). The treatments differed in effects on working memory but not other cognitive domains. Combination treatment improved working memory more than GUAN but was not significantly better than DMPH alone. Treatment did not fully normalize the initial deficit in ADHD relative to the comparison group.

**Conclusion:** Combined treatment with DMPH and GUAN yielded greater improvements in working memory than placebo or GUAN alone, but the combined treatment was not superior to DMPH alone and did not extend to other cognitive domains. Although GUAN may be a useful add-on treatment to psychostimulants, additional strategies appear to be necessary to achieve normalization of cognitive function in ADHD.

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Lancet. 2016 Mar;387:1240-50.

**ATTENTION DEFICIT HYPERACTIVITY DISORDER.**

**Thapar A, Cooper M.**

Attention deficit hyperactivity disorder (ADHD) is a childhood-onset neurodevelopmental disorder with a prevalence of 1.4-3.0%. It is more common in boys than girls. Comorbidity with childhood-onset neurodevelopmental disorders and psychiatric disorders is substantial. ADHD is highly heritable and multifactorial; multiple genes and non-inherited factors contribute to the disorder. Prenatal and perinatal factors have been implicated as risks, but definite causes remain unknown. Most guidelines recommend a stepwise approach to treatment, beginning with non-drug interventions and then moving to pharmacological treatment in those most severely affected. Randomised controlled trials show short-term benefits of stimulant medication and atomoxetine. Meta-analyses of blinded trials of non-drug treatments have not yet proven the efficacy of such interventions. Longitudinal studies of ADHD show heightened risk of multiple mental health and social difficulties as well as premature mortality in adult life.

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Learn Disabil Res Pract. 2016 Aug;31:142-55.

**IMPROVEMENT OF WORD PROBLEM SOLVING AND BASIC MATHEMATICS COMPETENCIES IN STUDENTS WITH ATTENTION DEFICIT/HYPERACTIVITY DISORDER AND MATHEMATICAL LEARNING DIFFICULTIES.**

**González-Castro P, Cueli M, Areces D, et al.**

Problem solving represents a salient deficit in students with mathematical learning difficulties (MLD) primarily caused by difficulties with informal and formal mathematical competencies. This study proposes a computerized intervention tool, the integrated dynamic representation (IDR), for enhancing the early learning of basic mathematical competencies and word problem solving skills. The goal was to compare and contrast the effects of IDR on the acquisition of informal and formal mathematical competencies in students with attention deficit/hyperactivity disorder (ADHD) and MLD. Participants were 216 students (6–9 years), who were classified into three groups: ADHD (n = 72), MLD (n = 82), ADHD and MLD (n = 62). They completed the Test of Early Mathematics Ability (Third Edition). The results showed that all three diagnosed groups improved significantly postintervention in all mathematical competencies, with the MLD-only group benefiting the most at posttest.

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Learn Disabil Q. 2016 Aug;39:182-90.

**VICTIMIZATION BY BULLYING AND ATTACHMENT TO PARENTS AND TEACHERS AMONG STUDENT WHO REPORT LEARNING DISORDERS AND/OR ATTENTION DEFICIT HYPERACTIVITY DISORDER .**

**Klomek AB, Kopelman-Rubin D, Al-Yagon M, et al.**

This is the first study examining the association between victimization by bullying and attachment to both parents and teachers among students who report Learning Disorders (LD) and/or Attention Deficit Hyperactivity Disorder (ADHD). A total of 1,691 seventh- and eighth-grade students in six junior high schools completed questionnaires about LD/ADHD diagnosis, victimization, and attachment to mother, father, and teacher. A regression analysis was conducted to estimate the probability for victimization (infrequent and frequent) through the various variables. Only students who reported both LD and ADHD (but not one of them) were at greater risk of frequent victimization compared with students who did not report LD/ADHD. In addition, having a secure attachment pattern to mother was associated with a decrease in the likelihood of being frequently bullied. Attachment patterns to father and teacher were not significantly associated with victimization group membership. Results suggest that children's perception of support and attachment to mother is important above and beyond their report on LD/ADHD diagnosis.

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Mol Psychiatry. 2016.

**RARE DNA VARIANTS IN THE BRAIN-DERIVED NEUROTROPHIC FACTOR GENE INCREASE RISK FOR ATTENTION-DEFICIT HYPERACTIVITY DISORDER: A NEXT-GENERATION SEQUENCING STUDY.**

**Hawi Z, Cummins TDR, Tong J, et al.**

Attention-deficit hyperactivity disorder (ADHD) is a prevalent and highly heritable disorder of childhood with negative lifetime outcomes. Although candidate gene and genome-wide association studies have identified promising common variant signals, these explain only a fraction of the heritability of ADHD. The observation that rare structural variants confer substantial risk to psychiatric disorders suggests that rare variants might explain a portion of the missing heritability for ADHD. Here we believe we performed the first large-scale next-generation targeted sequencing study of ADHD in 152 child and adolescent cases and 188 controls across an a priori set of 117 genes. A multi-marker gene-level analysis of rare (<1% frequency) single-nucleotide variants (SNVs) revealed that the gene encoding brain-derived neurotrophic factor (BDNF) was associated with ADHD at Bonferroni corrected levels. Sanger sequencing confirmed the existence of all novel rare BDNF variants. Our results implicate BDNF as a genetic risk factor for ADHD, potentially by virtue of its critical role in neurodevelopment and synaptic plasticity. Molecular Psychiatry advance online publication, 26 July 2016; doi:10.1038/mp.2016.117

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Nat Commun. 2016;7:11254.

**A SMALL NUMBER OF ABNORMAL BRAIN CONNECTIONS PREDICTS ADULT AUTISM SPECTRUM DISORDER.**

**Yahata N, Morimoto J, Hashimoto R, et al.**

Although autism spectrum disorder (ASD) is a serious lifelong condition, its underlying neural mechanism remains unclear. Recently, neuroimaging-based classifiers for ASD and typically developed (TD) individuals were developed to identify the abnormality of functional connections (FCs). Due to over-fitting and interferential effects of varying measurement conditions and demographic distributions, no classifiers have been strictly validated for independent cohorts. Here we overcome these difficulties by developing a novel machine-learning algorithm that identifies a small number of FCs that separates ASD versus TD. The classifier achieves high accuracy for a Japanese discovery cohort and demonstrates a remarkable degree of generalization for two independent validation cohorts in the USA and Japan. The developed ASD classifier does not distinguish individuals with major depressive disorder and attention-deficit hyperactivity disorder from their controls but moderately distinguishes patients with schizophrenia from their controls. The results leave open the viable possibility of exploring neuroimaging-based dimensions quantifying the multiple-disorder spectrum.

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Nat Neurosci. 2016 Jan;19:165-71.

**A NEUROMARKER OF SUSTAINED ATTENTION FROM WHOLE-BRAIN FUNCTIONAL CONNECTIVITY.**

**Rosenberg MD, Finn ES, Scheinost D, et al.**

Although attention plays a ubiquitous role in perception and cognition, researchers lack a simple way to measure a person's overall attentional abilities. Because behavioral measures are diverse and difficult to standardize, we pursued a neuromarker of an important aspect of attention, sustained attention, using functional magnetic resonance imaging. To this end, we identified functional brain networks whose strength during a sustained attention task predicted individual differences in performance. Models based on these networks generalized to previously unseen individuals, even predicting performance from resting-state connectivity alone. Furthermore, these same models predicted a clinical measure of attention--symptoms of attention deficit hyperactivity disorder--from resting-state connectivity in an independent sample of children and adolescents. These results demonstrate that whole-brain functional network strength provides a broadly applicable neuromarker of sustained attention.

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NeuroImage. 2016 Jan;124:1238-41.

**CONNECTED BRAINS AND MINDS--THE UMCD REPOSITORY FOR BRAIN CONNECTIVITY MATRICES .**

**Brown JA, Van Horn JD.**

We describe the USC Multimodal Connectivity Database (<http://umcd.humanconnectomeproject.org>), an interactive web-based platform for brain connectivity matrix sharing and analysis. The site enables users to download connectivity matrices shared by other users, upload matrices from their own published studies, or select a specific matrix and perform a real-time graph theory-based analysis and visualization of network properties. The data shared on the site span a broad spectrum of functional and structural brain connectivity information from humans across the entire age range (fetal to age 89), representing an array of different neuropsychiatric and neurodegenerative disease populations (autism spectrum disorder, ADHD, and APOE-4 carriers). An analysis combining 7 different datasets shared on the site illustrates the diversity of the data and the potential for yielding deeper insight by assessing new connectivity matrices with respect to population-wide network properties represented in the UMCD.

NeuroImage Clin. 2016;12:227-33.

**QUANTIFYING PATTERNS OF BRAIN ACTIVITY: DISTINGUISHING UNAFFECTED SIBLINGS FROM PARTICIPANTS WITH ADHD AND HEALTHY INDIVIDUALS.**

**Wolfers T, van Rooij D, Oosterlaan J, et al.**

Attention-deficit/hyperactivity disorder (ADHD) is one of the most prevalent and heritable psychiatric disorders. While previous studies have focussed on mapping focal or connectivity differences at the group level, the present study employed pattern recognition to quantify group separation between unaffected siblings, participants with ADHD, and healthy controls on the basis of spatially distributed brain activations. This was achieved using an fMRI-adapted version of the Stop-Signal Task in a sample of 103 unaffected siblings, 184 participants with ADHD, and 128 healthy controls. We used activation maps derived from three task regressors as features in our analyses employing a Gaussian process classifier. We showed that unaffected siblings could be distinguished from participants with ADHD (area under the receiver operating characteristic curve (AUC) = 0.65,  $p = 0.002$ , 95% Modified Wald CI: 0.59-0.71 AUC) and healthy controls (AUC = 0.59,  $p = 0.030$ , 95% Modified Wald CI: 0.52-0.66 AUC), although the latter did not survive correction for multiple comparisons. Further, participants with ADHD could be distinguished from healthy controls (AUC = 0.64,  $p = 0.001$ , 95% Modified Wald CI: 0.58-0.70 AUC). Altogether the present results characterise a pattern of frontolateral, superior temporal and inferior parietal expansion that is associated with risk for ADHD. Unaffected siblings show differences primarily in frontolateral regions. This provides evidence for a neural profile shared between participants with ADHD and their healthy siblings.

Neuropsychopharmacology. 2016.

**FUNCTIONAL IMPACT OF AN ADHD-ASSOCIATED DIRAS2 PROMOTER POLYMORPHISM.**

**Grünewald L, Landaas ET, Geissler J, et al.**

The DIRAS2 gene is coding for a small Ras GTPase with so far unknown function. In a previous study, we described the association of DIRAS2 rs1412005, as well as a haplotype containing this polymorphism and located in the promoter region of this gene with attention-deficit/hyperactivity disorder (ADHD). In the present study, we searched for rare variants within or near the DIRAS2 gene that might be associated with ADHD using next-generation sequencing. As we were not able to detect any rare variants associated with the disease, we sought to establish a functional role of DIRAS2 rs1412005 on the molecular or systems level. First, we investigated whether it has an influence on gene expression by means of a luciferase-based promoter assay. We could demonstrate that the minor risk allele goes along with the increased expression of the reporter gene. Next, we aimed to identify differences in response inhibition between risk-allele and non-risk allele carriers in children suffering from ADHD and healthy control individuals by analyzing event-related potentials in the electroencephalogram during a Go/NoGo task. Risk-allele carriers showed a changed NoGo anteriorization. Therefore, our results suggest an impact of the investigated polymorphism

on the prefrontal response control in children with ADHD. These results imply that the promoter polymorphism is indeed the associated as well as in itself a causal variant. Further research is thus warranted to clarify the mechanisms linking DIRAS2 to ADHD. Neuropsychopharmacology advance online publication, 27 July 2016; doi:10.1038/npp.2016.113

Neurosci Lett. 2016 Mar;617:195-200.

**INCREASED URINARY 6-HYDROXYMELATONINSULFATE LEVELS IN ATTENTION DEFICIT HYPERACTIVITY DISORDER DIAGNOSED CHILDREN AND ADOLESCENT.**

**Buber A, Cakaloz B, Isildar Y, et al.**

There are some studies in attention deficit hyperactivity disorder (ADHD) which note altered circadian rhythms, suggesting abnormalities in melatonin physiology. In order to better characterize the possible melatonin alteration in ADHD, in this study we aimed to detect daytime, nighttime and 24 h levels of 6-hydroxymelatonininsulfate (6-OH MS) in the patients diagnosed with ADHD. Twenty-seven patients between 6 and 16 years-old, who had been diagnosed initially with ADHD, but without other physical and psychiatric disease history and who had not taken psychotropic pharmacotherapy for six months, plus 28 healthy volunteer controls, were included in the study. Urine samples were collected during the whole 24 h cycle, daytime and nighttime separately to assess the time-dependent excretion of the 6-OH MS, which is the main urine metabolite of melatonin. The Enzyme-Linked Immunosorbent Assay (ELISA) method was used for measuring the urine 6-OH MS level. Daytime (15.4 (8.9-24.8) ng/ml vs 6.9 (2.5-15.9) ng/ml,  $p=0.002$ ), nighttime (102.9 (65.3-197.7) ng/ml vs 61.5 (37.2-114.4) ng/ml,  $p=0.012$ ) and 24 h (54.1 (34.6-83.9) ng/ml vs 27.3 (14.3-48.9) ng/ml,  $p=0.000$ ) 6-OH MS levels median (25p-75p) were found to be significantly higher in the ADHD group. After adjustment for age and sex, there was a statistically significant difference between the ADHD group (59.8 +/- 4.9) and control group (33.8 +/- 4.8) in 24-h 6-OH MS levels ( $F(1, 51)=13.673$ ,  $p=.001$ , partial  $\eta^2=.211$ ). There was no relationship between 6-OH MS levels and Conners Parent Rating Scale short form subscale scores for the ADHD group. These findings indicate that melatonin production is increased in ADHD cases. Further research is needed to determine and thereby understand the mechanisms underlying the higher melatonin production, to assess the impact of altered melatonin on the pathophysiology of ADHD.

Neurosci Lett. 2016 Jan;612:132-37.

**A META-ANALYSIS OF MISMATCH NEGATIVITY IN CHILDREN WITH ATTENTION DEFICIT-HYPERACTIVITY DISORDERS.**

**Cheng CH, Chan PY, Hsieh YW, et al.**

Mismatch negativity (MMN) is an optimal neurophysiological signal to assess the integrity of auditory sensory memory and involuntary attention switch. The generation of MMN is independent of overt behavioral requirements, concentration or motivation, and thus serves as a suitable tool to study the perceptual function in children with attention deficit-hyperactivity disorders (ADHD). It remains unclear whether ADHD children showed altered MMN responses. Therefore we performed a meta-analysis of peer-reviewed MMN studies that had targeted both typically developed and ADHD children to examine the pooled effect size. The published articles between 1990 and 2014 were searched in PubMed, Medline, Cochrane, and CINAHL. The mean effect size and a 95% confidence interval (CI) were estimated. Six studies, consisting of 10 individual investigations, were included in the final analysis. A significant effect size of 0.28 was found ( $p=0.028$ , 95% CI at 0.03-0.53). These results were also free from publication bias or heterogeneity. In conclusion, our meta-analysis results suggest ADHD children demonstrated a reduced MMN amplitude compared to healthy controls.

Neuroscience. 2016;333:27-34.

**SACCADE ADAPTATION IN YOUNG PEOPLE DIAGNOSED WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER COMBINED TYPE.**

**Connolly AJ, Rinehart NJ, Fielding J.**

Growing evidence suggests Attention Deficit Hyperactivity Disorder (ADHD) often co-occurs with Autism Spectrum Disorder (ASD), and a better understanding of the nature of their overlap, including at a neurobiological level, is needed. Research has implicated cerebellar-networks as part of the neural-circuitry disrupted in ASD, but little research has been carried out to investigate this in ADHD. We investigated cerebellar integrity using a double-step saccade adaptation paradigm in a group of male children age 8-15 (n=12) diagnosed with ADHD-Combined Type (-CT). Their performance was compared to a group of age and IQ-matched typically developing (TD) controls (n=12). Parent reported symptoms of ADHD-CT and ASD were measured, along with motor proficiency (Movement ABC-2). We found, on average, the adaptation of saccade gain was reduced for the ADHD-CT group compared to the TD group. Greater saccadic gain change (adaptation) was also positively correlated with higher Movement ABC-2 total and balance scores among the ADHD-CT participants. These differences suggest cerebellar networks underlying saccade adaptation may be disrupted in young people with ADHD-CT. Though our findings require further replication with larger samples, they suggest further research into cerebellar dysfunction in ADHD-CT, and as a point of neurobiological overlap with ASD, may be warranted.

Neuroscience. 2016;334:47-54.

**VOLUNTARY SACCADDES IN ATTENTION-DEFICIT/HYPERACTIVITY DISORDER: LOOKING INTO THE RELATIONSHIP BETWEEN MOTOR IMPAIRMENT AND AUTISM SPECTRUM DISORDER SYMPTOMS.**

**Connolly AJ, Rinehart NJ, Johnson B, et al.**

Although there is little overlap in core diagnostic criteria for ADHD and Autism Spectrum Disorder (ASD), ASD symptoms are estimated to co-occur in children with ADHD in 20-50% of cases. As motor control deficits are common to both disorders, we investigated the impact of ASD symptoms on ocular motor control in children with Attention Deficit Hyperactivity Disorder-Combined Type (ADHD-CT), using a cued saccade paradigm sensitive to cerebellar ocular motor impairment in ASD. Basic saccade metrics (latency, velocity and accuracy), trial-to-trial variability, and main sequences relationships (saccade velocity for a given amplitude) were assessed, for 14 males with ADHD-CT and 14 typically developing (TD) males (aged 8-14, IQ>80). Our results revealed that saccade profiles of the ADHD-CT group showed a pattern of hypermetria and altered main sequence. As the cerebellum is crucially involved in the regulation of saccade parameters, we propose that this pattern of deficit in ADHD-CT is consistent with the widely reported morphological abnormalities in ocular motor vermis (cerebellar lobules VI-VII) in ADHD-CT and ASD.

Nord J Psychiatry. 2016;70:133-39.

**NON-OBSESSIVE-COMPULSIVE ANXIETY DISORDERS IN CHILD AND ADOLESCENT MENTAL HEALTH SERVICES--ARE THEY UNDERDIAGNOSED, AND HOW ACCURATE IS REFERRAL INFORMATION?**

**Hansen BH, Oerbeck B, Skirbekk B, et al.**

**BACKGROUND:** Previous studies have reported low prevalence of non-obsessive-compulsive (OCD) anxiety disorders in child and adolescent mental health services (CAMHSs), suggesting that these disorders may go unrecognized. Possible reasons may be lack of routinely used standardized diagnostic instruments, and/or an under-reporting of anxiety symptoms in the referral information.

**AIMS:** To examine the frequency of non-OCD anxiety disorders in referred children based on a standardized diagnostic interview, to compare the results with data from the Norwegian Patient Register (NPR), and to explore the correspondence between anxiety as a referral symptom and anxiety as a diagnosis, and the influence of heterotypic co-morbidity on this correspondence.



**METHODS:** Parents of 407 consecutive referrals to CAMHS aged 7-13 years were interviewed with the semi-structured diagnostic interview Kiddie-SADS-PL at the time of admittance. Referral symptoms were collected from national referral forms.

**RESULTS:** A total of 133 referred children (32.7%) met the criteria for a non-OCD anxiety disorder compared with about 5% in the NPR. Half of those who met diagnostic criteria for an anxiety disorder did not have anxiety as a referral symptom. Co-morbid ADHD or disruptive disorder was significantly associated with a lower probability of having anxiety as a referral symptom.

**CONCLUSIONS:** The use of a standardized diagnostic interview in consecutively referred children yielded significantly higher rates of anxiety disorders than the NPR prevalence rates. Co-morbid ADHD or disruptive disorder may contribute to the underdiagnosing of anxiety disorders. Diagnostic instruments covering the whole range of child psychiatric symptoms should be implemented routinely in CAMHS.

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Nord J Psychiatry. 2016;70:146-55.

**PSYCHIATRIC DISORDERS IN DANISH CHILDREN AGED 5-7 YEARS: A GENERAL POPULATION STUDY OF PREVALENCE AND RISK FACTORS FROM THE COPENHAGEN CHILD COHORT (CCC 2000).**

**Elberling H, Linneberg A, Rask CU, et al.**

**BACKGROUND:** Knowledge about the presentation of psychopathology in preschool age and associated risk factors is fundamental to preventive intervention before schooling.

**AIMS:** To investigate the full spectrum of psychiatric diagnoses in general population children at the period of transition from preschool to school.

**METHODS:** A sample of 1585 children from the Copenhagen Child Cohort, CCC2000 aged 5-7 years was assessed using the Development and Well-Being Assessment (DAWBA) with diagnostic classification by experienced clinicians. Perinatal, sociodemographic and socio-economic data was obtained from Danish national registries.

**RESULTS:** The prevalence of any ICD-10 psychiatric disorder was 5.7% (95%CI: 4.4-7.1). Pervasive developmental disorders (PDD) were found in 1.3% (95%CI: 0.8-1.8) and behavioural and hyperkinetic disorders were found in 1.5% (95%CI: 0.9-2.1) and 1.0% (95%CI: 0.4-1.6), respectively. Emotional disorders were found in 2.9% (95%CI: 1.9-4.0). More boys were diagnosed with PDD, behavioural disorders and tics. No gender differences were found in hyperactivity disorders (HD) and emotional disorders. Co-morbidity was frequent, in particular between HD and PDD, but also between HD and emotional disorder and behavioural disorder. Teenage mothers, single parents and low household income the first two years after the child's birth were associated with a three- to fourfold increased risk of psychiatric disorder in the child at age 5-7 years.

**CONCLUSION:** The study results point to two "windows of opportunity" for prevention. In the earliest postnatal years, prevention should target families at socio-economic risk; and in the years before schooling, intervention should focus on children with symptoms of PDD, HD, and behavioural disorders.

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Nord J Psychiatry. 2016;70:1-9.

**THE GENETICS AND NEUROBIOLOGY OF ESSENCE: THE THIRD BIRGIT OLSSON LECTURE.**

**Bourgeron T.**

ESSENCE refers to early symptomatic syndromes eliciting neurodevelopmental clinical examinations. It includes a broad range of early onset neurodevelopmental disorders affecting more than 10% of children before 5 years of age. ESSENCE includes among others attention deficit hyperactivity disorder (ADHD), intellectual disability (ID) and autism spectrum disorders (ASD). Some degree of disability is the rule rather than the exception. The causes are heterogeneous ranging from extreme social deprivation, pre- and perinatal risk factors, genetic and metabolic diseases, immune and infectious disorders, nutritional factors, physical trauma, and postnatal toxic and environmental factors (and combinations/interactions of some or several of these). Treatments often involve a combination of psychoeducational interventions, home- and school-based programmes, and medication. Here, I will first briefly review our main knowledge on the biological pathways associated with early onset neurodevelopmental disorders and will provide useful links

to be informed of the progress in the field. Five main pathways are associated with ASD and ID: chromatin remodelling, cytoskeleton dynamics, mRNA translation, metabolism and synapse formation/function. I will then detail three propositions coming from institutions, researchers and/or communities of patients and families to foster research: 1) to use more dimensional and quantitative data than diagnostic categories; 2) to increase data sharing and research on genetic and brain diversity in human populations; 3) to involve patients and relatives as participants for research. Finally, I will provide examples of very stimulating initiatives towards a more inclusive world for individuals with ESSENCE.

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Nurs Stand. 2016 Feb;30:32-33.

**MEDS ARE NO PANACEA FOR CHILDREN WHO MIGHT HAVE ADHD.**

**Owen M.**

I agree caution needs to be exercised in using methylphenidate, most commonly known as Ritalin, for attention deficit hyperactivity disorder in children, (clinical update, January 20)

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Oman Medical Journal. 2016;31:258-62.

**PSYCHIATRIC DISORDERS IN CHILDREN AND ADOLESCENTS ATTENDING PEDIATRIC OUT PATIENT DEPARTMENTS OF TERTIARY HOSPITALS.**

**Jesmin A, Mullick MSI, Zillur Rahman KM, et al.**

**Objectives:** Psychiatric disorders are increasingly recognized among children and adolescents in Bangladesh. Psychiatric disorders are more common in children with chronic and acute pediatric disorders. Our study was designed to determine the psychiatric disorders among children and adolescents attending pediatric outpatient departments of tertiary care hospitals.

**Methods:** This cross-sectional study was carried out from July 2012 to February 2013 in pediatric outpatient departments of three prime tertiary level hospitals of Dhaka, Bangladesh. A purposive sampling technique was used. A total of 240 male and female children aged 5 to 16 years old were included in the study. We used a semi-structured questionnaire to obtain sociodemographic and other relevant clinical information about the children and their families from their parents or caregivers and a validated parent version of the Bangla Development and Well-Being Assessment (DAWBA) for measuring psychopathology.

**Results:** The mean age of the children was 9.0-| 2.6 years. The majority (71%) of children were in the 5-10 year age group. The male/female ratio was 1.2: 1. Among the respondents, 18% were found to have a psychiatric disorder. Behavioral disorders, emotional disorders, and developmental disorders were found in 9.0%, 15.0% and 0.4% respectively. Hyperkinetic disorder was the single most frequent (5.0%) psychiatric disorder.

**Conclusions:** A significant number of children were found to have psychiatric disorders. Our study indicates the importance of identification and subsequent management of psychiatric conditions among the pediatric population.

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Pediatrics. 2016;138.

**CHILDHOOD EPILEPSY, FEBRILE SEIZURES, AND SUBSEQUENT RISK OF ADHD.**

**Bertelsen EN, Larsen JT, Petersen L, et al.**

**OBJECTIVES:** Epilepsy, febrile seizures, and attention-deficit/hyperactivity disorder (ADHD) are disorders of the central nervous system and share common risk factors. Our goal was to examine the association in a nationwide cohort study with prospective follow-up and adjustment for selected confounders. We hypothesized that epilepsy and febrile seizures were associated with subsequent ADHD.

**METHODS:** A population-based cohort of all children born in Denmark from 1990 through 2007 was followed up until 2012. Incidence rate ratios (IRRs) and 95% confidence intervals (95% CIs) for ADHD were estimated by using Cox regression analysis, comparing children with epilepsy and febrile seizure with those without

these disorders, adjusted for socioeconomic and perinatal risk factors, as well as family history of neurologic and psychiatric disorders.

**RESULTS:** A total of 906 379 individuals were followed up for 22 years (10 million person-years of observation); 21 079 individuals developed ADHD. Children with epilepsy had a fully adjusted IRR of ADHD of 2.72 (95% CI, 2.53-2.91) compared with children without epilepsy. Similarly, in children with febrile seizure, the fully adjusted IRR of ADHD was 1.28 (95% CI, 1.20-1.35). In individuals with both epilepsy and febrile seizure, the fully adjusted IRR of ADHD was 3.22 (95% CI, 2.72-3.83).

**CONCLUSIONS:** Our findings indicate a strong association between epilepsy in childhood and, to a lesser extent, febrile seizure and subsequent development of ADHD, even after adjusting for socioeconomic and perinatal risk factors, and family history of epilepsy, febrile seizures, or psychiatric disorders.

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Pediatrics. 2016;138.

#### **IMPACT OF A WEB-PORTAL INTERVENTION ON COMMUNITY ADHD CARE AND OUTCOMES.**

**Epstein JN, Kelleher KJ, Baum R, et al.**

**BACKGROUND:** The quality of care for children with attention-deficit/hyperactivity disorder (ADHD) delivered in community-based pediatric settings is often poor. Interventions have been developed to improve community-based ADHD care but have not demonstrated that better care results in improved patient outcomes. The objective of this study was to determine whether an ADHD quality improvement (QI) intervention for community-based pediatric practices improves patient outcomes.

**METHODS:** A cluster randomized controlled trial was conducted in which 50 community-based pediatric primary care practices (213 providers) were randomized either to receive a technology-assisted QI intervention or to a control condition. The intervention consisted of 4 training sessions, office flow modification, guided QI, and an ADHD Internet portal to assist with treatment monitoring. ADHD treatment processes and parent- and teacher-rated ADHD symptoms over the first year of treatment were collected for 577 patients.

**RESULTS:** Intent-to-treat analyses examining outcomes of all children assessed for ADHD were not significant ( $b = -1.97$ ,  $P = .08$ ). However, among the 373 children prescribed ADHD medication, there was a significant intervention effect ( $b = -2.42$ ,  $P = .04$ ) indicating greater reductions in parent ratings of ADHD symptoms after treatment among patients treated by intervention physicians compared with patients treated at control practices. There were no group differences on teacher ratings of ADHD symptoms. ADHD treatment care around medication was significantly better at intervention practices compared with control practices.

**CONCLUSIONS:** A technology-assisted QI intervention improved some ADHD care quality and resulted in additional reductions in parent-rated ADHD symptoms among patients prescribed ADHD medications.

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Pediatrics. 2016;138.

#### **NEURODEVELOPMENTAL DISORDERS OR EARLY DEATH IN SIBLINGS OF CHILDREN WITH CEREBRAL PALSY.**

**Tollanes MC, Wilcox AJ, Stoltenberg C, et al.**

**OBJECTIVES:** To explore the presence of shared underlying causes of cerebral palsy (CP) and other neurodevelopmental disorders, by examining risks of other disorders in siblings of children with CP.

**METHODS:** We used Norwegian national registries to identify 1.4 million pairs of full siblings (singletons) and 28 000 sets of twins born from 1967 to 2006, identify stillbirths and neonatal deaths, and find individuals with CP, epilepsy, intellectual disability, autism spectrum disorders, attention-deficit/hyperactivity disorder, blindness, deafness, schizophrenia, and bipolar disorder. Associations between CP in 1 sibling and neurodevelopmental disorders or early death in other siblings were estimated using logistic regression models.

**RESULTS:** There were 5707 neonatal survivors (beyond 28 days) with CP (2.5/1000). These children had substantial comorbidity (eg, 29% had epilepsy). Singleton siblings of (singleton) children with CP had increased risks of neurodevelopmental problems, including epilepsy (odds ratio [OR], 1.8 [95% confidence

interval (CI), 1.5-2.5]), intellectual disability (OR, 2.3 [95% CI, 1.8-2.9]), autism spectrum disorders (OR, 1.6 [95% CI, 1.1-2.2]), attention deficit/hyperactivity disorder (OR 1.3 [95% CI, 1.1-1.6]), blindness (OR 2.4 [95% CI, 1.1-5.4]), and schizophrenia (OR 2.0 [95% CI, 1.2-3.2]). There was no increase in risk of bipolar disorder (OR 1.0 [95% CI, 0.6-1.6]). Families with children with CP also had increased risk of losing another child in the perinatal period (stillbirth OR, 1.8 [95% CI, 1.5- 2.3]; neonatal death OR, 1.7 [95% CI, 1.3-2.2]). Associations were stronger within sets of twins.

**CONCLUSIONS:** Siblings of a child with CP were at increased risk for a variety of other neurodevelopmental morbidities, as well as early death, indicating the presence of shared underlying causes.

PeerJ. 2015;2015.

#### NEURODEVELOPMENTAL PROBLEMS AND EXTREMES IN BMI.

**Kerekes N, Tajnia A, Lichtenstein P, et al.**

**Background.** Over the last few decades, an increasing number of studies have suggested a connection between neurodevelopmental problems (NDPs) and body mass index (BMI). Attention deficit/hyperactivity disorder (ADHD) and autism spectrum disorders (ASD) both seem to carry an increased risk for developing extreme BMI. However, the results are inconsistent, and there have been only a few studies of the general population of children.

**Aims.** We had three aims with the present study: (1) to define the prevalence of extreme (low or high) BMI in the group of children with ADHD and/or ASDs compared to the group of children without these NDPs; (2) to analyze whether extreme BMI is associated with the subdomains within the diagnostic categories of ADHD or ASD; and (3) to investigate the contribution of genetic and environmental factors to BMI in boys and girls at ages 9 and 12. Method. Parents of 9- or 12-year-old twins (n = 12,496) were interviewed using the Autism-Tics, ADHD and other Comorbidities (A-TAC) inventory as part of the Child and Adolescent Twin Study in Sweden (CATSS). Univariate and multivariate generalized estimated equation models were used to analyze associations between extremes in BMI and NDPs.

**Results.** ADHD screen-positive cases followed BMI distributions similar to those of children without ADHD or ASD. Significant association was found between ADHD and BMI only among 12-year-old girls, where the inattention subdomain of ADHD was significantly associated with the high extreme BMI. ASD scores were associated with both the low and the high extremes of BMI. Compared to children without ADHD or ASD, the prevalence of ASD screen-positive cases was three times greater in the high extreme BMI group and double as much in the low extreme BMI group. Stereotyped and repetitive behaviors were significantly associated with high extreme BMIs.

**Conclusion.** Children with ASD, with or without coexisting ADHD, are more prone to have low or high extreme BMIs than children without ADHD or ASD.

PLoS ONE. 2016;11.

#### EMOTION REGULATION DIFFICULTIES IN BOYS WITH OPPOSITIONAL DEFIANT DISORDER/CONDUCT DISORDER AND THE RELATION WITH COMORBID AUTISM TRAITS AND ATTENTION DEFICIT TRAITS.

**Schoorl J, Van Rijn S, De Wied M, et al.**

Previous research has pointed towards a link between emotion dysregulation and aggressive behavior in children. Emotion regulation difficulties are not specific for children with persistent aggression problems, i.e. oppositional defiant disorder or conduct disorder (ODD/CD), children with other psychiatric conditions, such as autism spectrum disorders or attention-deficit/hyperactivity disorder, have emotion regulation difficulties too. On a behavioral level some overlap exists between these disorders and comorbidity is high. The aim of this study was therefore twofold: 1) to examine emotion regulation difficulties in 65 boys with ODD/CD in comparison to a non-clinical control group (NC) of 38 boys (8-12 years) using a performance measure (Ultimatum Game), parent report and self-report, and 2) to establish to what extent emotion regulation in the ODD/CD group was correlated with severity of autism and/or attention deficit traits. Results on the Ultimatum Game showed that the ODD/CD group rejected more ambiguous offers than the NC group, which is seen as

an indication of poor emotion regulation. Parents also reported that the ODD/CD group experienced more emotion regulation problems in daily life than the NC group. In contrast to these cognitive and behavioral measures, self-reports did not reveal any difference, indicating that boys with ODD/CD do not perceive themselves as having impairments in regulating their emotions. Emotional decision making within the ODD/CD group was not related to variation in autism or attention deficit traits. These results support the idea that emotion dysregulation is an important problem within ODD/CD, yet boys with ODD/CD have reduced awareness of this.

PLoS ONE. 2016;11.

**PERIPHERAL ATTENTIONAL TARGETS UNDER COVERT ATTENTION LEAD TO PARADOXICALLY ENHANCED ALPHA DESYNCHRONIZATION IN NEUROFIBROMATOSIS TYPE 1.**

**Silva G, Ribeiro MJ, Costa GN, et al.**

The limited capacity of the human brain to process the full extent of visual information reaching the visual cortex requires the recruitment of mechanisms of information selection through attention. Neurofibromatosis type-1 (NF1) is a neurodevelopmental disease often exhibiting attentional deficits and learning disabilities, and is considered to model similar impairments common in other neurodevelopmental disorders such as autism. In a previous study, we found that patients with NF1 are more prone to miss targets under overt attention conditions. This finding was interpreted as a result of increased occipito-parietal alpha oscillations. In the present study, we used electroencephalography (EEG) to study alpha power modulations and the performance of patients with NF1 in a covert attention task. Covert attention was required in order to perceive changes (target offset) of a peripherally presented stimulus. Interestingly, alpha oscillations were found to undergo greater desynchronization under this task in the NF1 group compared with control subjects. A similar pattern of desynchronization was found for beta frequencies while no changes in gamma oscillations could be identified. These results are consistent with the notion that different attentional states and task demands generate different patterns of abnormal modulation of alpha oscillatory processes in NF1. Under covert attention conditions and while target offset was reported with relatively high accuracy (over 90% correct responses), excessive desynchronization was found. These findings suggest an abnormal modulation of oscillatory activity and attentional processes in NF1. Given the known role of alpha in modulating attention, we suggest that alpha patterns can show both abnormal increases and decreases that are task and performance dependent, in a way that enhanced alpha desynchronization may reflect a compensatory mechanism to keep performance at normal levels. These results suggest that dysregulation of alpha oscillations may occur in NF1 both in terms of excessive or diminished activation patterns.

PLoS ONE. 2016;11.

**ENURESIS AND HYPERACTIVITY-INATTENTION IN EARLY ADOLESCENCE: FINDINGS FROM A POPULATION-BASED SURVEY IN TOKYO (TOKYO EARLY ADOLESCENCE SURVEY).**

**Kanata S, Koike S, Ando S, et al.**

**Background** Enuresis (9% at age 9.5) negatively affects children's psychosocial status. Clinically-diagnosed enuresis (2% at the age) is associated with hyperactivity-inattention, and common neural bases have been postulated to underlie this association. It is, however, unclear whether this association is applicable to enuresis overall among the general population of early adolescents when considered comorbid behavioral problems. We aimed to examine whether enuresis correlates with hyperactivity-inattention after controlling for the effects of other behavioral problems.

**Methods** Participants were 4,478 children (mean age 10.2 - 0.3 years old) and their parents from the Tokyo Early Adolescence Survey (T-EAS), a population-representative cross-sectional study conducted in Tokyo, Japan conducted from 2012 to 2015. Children's enuresis and behavioral problems, including hyperactivity-inattention (as measured by the Strength and Difficulties Questionnaire), were examined using parent-reporting questionnaires. Multivariate linear regression was used to explore whether enuresis predicts hyperactivity-inattention.



**Results** The hyperactivity-inattention score was significantly higher in the enuretic group than the non-enuretic group (enuretic: M (SD) = 3.8 (2.3), non-enuretic: M (SD) = 3.0 (2.1), Hedge's  $g = 0.39$ ,  $p < .001$ ). This association remained significant even after controlling for other behavioral problems and including sex, age, intelligence quotient (IQ), low birth weight and parents' education ( $+ = .054$  [95% CI: .028-.080],  $p < .001$ ).

**Conclusions** Enuresis was independently associated with hyperactivity-inattention in early adolescents among general population even when other behavioral problems were considered. These results suggest that, as with clinically-diagnosed cases, enuresis may predict need for screening and psychosocial support for hyperactivity-inattention.

PLoS ONE. 2016;11:e0145288.

**DESYNCHRONIZATION OF THETA-PHASE GAMMA-AMPLITUDE COUPLING DURING A MENTAL ARITHMETIC TASK IN CHILDREN WITH ATTENTION DEFICIT/HYPERACTIVITY DISORDER.**

*Kim JW, Kim BN, Lee J, et al.*

**INTRODUCTION:** Theta-phase gamma-amplitude coupling (TGC) measurement has recently received attention as a feasible method of assessing brain functions such as neuronal interactions. The purpose of this electroencephalographic (EEG) study is to understand the mechanisms underlying the deficits in attentional control in children with attention deficit/hyperactivity disorder (ADHD) by comparing the power spectra and TGC at rest and during a mental arithmetic task.

**METHODS:** Nineteen-channel EEGs were recorded from 97 volunteers (including 53 subjects with ADHD) from a camp for hyperactive children under two conditions (rest and task performance). The EEG power spectra and the TGC data were analyzed. Correlation analyses between the Intermediate Visual and Auditory (IVA) continuous performance test (CPT) scores and EEG parameters were performed.

**RESULTS:** No significant difference in the power spectra was detected between the groups at rest and during task performance. However, TGC was reduced during the arithmetic task in the ADHD group compared with the normal group ( $F = 16.70$ ,  $p < 0.001$ ). The TGC values positively correlated with the IVA CPT scores but negatively correlated with theta power.

**CONCLUSIONS:** Our findings suggest that desynchronization of TGC occurred during the arithmetic task in ADHD children. TGC in ADHD children is expected to serve as a promising neurophysiological marker of network deactivation during attention-demanding tasks.

Prescriber. 2016;27:37-38.

**GUANFACINE TO CONTROL ADHD IN CHILDREN AND ADOLESCENTS.**

*Chaplin S.*

Guanfacine (Intuniv) is an alpha 2A agonist indicated for the treatment of attention deficit hyperactivity disorder (ADHD) in children and adolescents for whom stimulants are not appropriate. This article discusses the indications, monitoring requirements and clinical trial results.

Psychiatr Invest. 2016;13:427-33.

**GENETIC VARIATIONS IN ATTENTION DEFICIT HYPERACTIVITY DISORDER SUBTYPES AND TREATMENT RESISTANT CASES.**

*Unal D, Unal MF, Alikasifoglu M, et al.*

**Objective** We evaluated the distribution of alpha-2A adrenergic receptor (ADRA2A) and catechol-o-methyltransferase (COMT) single nucleotide polymorphisms (SNPs) among ADHD subtypes and other homogeneous patient populations including treatment-resistant cases and patients with high symptom severity.

**Methods** 121 ADHD patients aged 6–18 years were included in the study. Diagnosis and subtypes designation were confirmed using the Kiddie Schedule for Affective Disorders and Schizophrenia (K-SADS) and symptoms were evaluated using the Conners' Parent (CPRS) and Teacher Rating Scales (CTRS). The response to methylphenidate was assessed objectively using the Clinical Global Impression-Severity Scale (CGI-S) and Global Assessment of Functioning Scale (GAS) as well as the Continuous Performance (CPT) and Trail Making tests (TMT-A, B). Patients were genotyped for ADRA2A (rs1800544) and COMT (rs4680) SNPs by PCR/RFLP and compared to a gender-matched control group.

**Results** Although there was no association of COMT (rs4680) SNP with symptoms or diagnosis, the ADRA2A polymorphism, low socioeconomic status (SES), and comorbid psychiatric diagnosis were all associated with poor response to methylphenidate in logistic regression analysis.

**Conclusion** Clinicians may consider adjuvant strategies when these negative factors are present to increase the success of tailored ADHD treatments in the future.

Psychiatry Res. 2016;244:382-87.

**GENDER RATIOS OF ADMINISTRATIVE PREVALENCE AND INCIDENCE OF ATTENTION-DEFICIT/HYPERACTIVITY DISORDER (ADHD) ACROSS THE LIFESPAN: A NATIONWIDE POPULATION-BASED STUDY IN TAIWAN.**

**Huang CLC, Weng SF, Ho CH.**

To verify the hypothesis that there is different gender ratio of attention-deficit/hyperactivity disorder (ADHD) among adults compared to children and adolescents in the clinical setting among Asian population. The nationwide population-based database containing data on enrollees in the National Health Insurance program in Taiwan during 2000–2007 was used in this study, and we investigated the lifetime gender ratios of administrative prevalence and incidence in healthcare-seeking ADHD patients (n=228,029). The male-to-female ratios of diagnosed incidence and prevalence of child/adolescent ADHD (age <20 years) ranged from 3.39 to 4.07 and 3.87–4.31, respectively. The male-to-female ratios of diagnosed incidence and prevalence of ADHD in the adult group (age 20–65 years) ranged from 0.24 to 0.76 and 0.35–0.98, respectively. In conclusion, there was substantially increased female-to-male ratio in adults ADHD compared to children and adolescents in the clinical setting. Further researches on the management and mechanism are needed.

Psychol Med. 2016 Aug;46:2363-73.

**DEFINING THE NEUROANATOMIC BASIS OF MOTOR COORDINATION IN CHILDREN AND ITS RELATIONSHIP WITH SYMPTOMS OF ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.**

**Shaw P, Weingart D, Bonner T, et al.**

**Background:** When children have marked problems with motor coordination, they often have problems with attention and impulse control. Here, we map the neuroanatomic substrate of motor coordination in childhood and ask whether this substrate differs in the presence of concurrent symptoms of attention-deficit/hyperactivity disorder (ADHD).

**Method:** Participants were 226 children. All completed Diagnostic and Statistical Manual of Mental Disorders, fifth edition (DSM-5)-based assessment of ADHD symptoms and standardized tests of motor coordination skills assessing aiming/catching, manual dexterity and balance. Symptoms of developmental coordination disorder (DCD) were determined using parental questionnaires. Using 3 Tesla magnetic resonance data, four latent neuroanatomic variables (for the cerebral cortex, cerebellum, basal ganglia and thalamus) were extracted and mapped onto each motor coordination skill using partial least squares pathway modeling.

**Results:** The motor coordination skill of aiming/catching was significantly linked to latent variables for both the cerebral cortex ( $t = 4.31$ ,  $p < 0.0001$ ) and the cerebellum ( $t = 2.31$ ,  $p = 0.02$ ). This effect was driven by the premotor/motor cortical regions and the superior cerebellar lobules. These links were not moderated by the severity of symptoms of inattention, hyperactivity and impulsivity. In categorical analyses, the DCD group showed atypical reduction in the volumes of these regions. However, the group with DCD alone did not differ significantly from those with DCD and co-morbid ADHD.

**Conclusions:** The superior cerebellar lobules and the premotor/motor cortex emerged as pivotal neural substrates of motor coordination in children. The dimensions of these motor coordination regions did not differ significantly between those who had DCD, with or without co-morbid ADHD.

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Psychol Addict Behav. 2016 Aug;30:588-600.

**CIGARETTE SMOKING AND ADHD: AN EXAMINATION OF PROGNOSTICALLY RELEVANT SMOKING BEHAVIORS AMONG ADOLESCENTS AND YOUNG ADULTS.**

**Rhodes JD, Pelham WE, Gnagy EM, et al.**

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Res Autism Spectr Disord. 2016;31:11-18.

**THE COMORBIDITY OF ADHD IN CHILDREN DIAGNOSED WITH AUTISM SPECTRUM DISORDER.**

**Stevens T, Peng L, Barnard-Brak L.**

**Background** The purpose of the present study was to investigate the comorbid presence of ADHD in a population of children diagnosed with ASD in a nationally representative sample. Comorbidity estimates range widely, with estimates as low as 37% and as high as 78%.

**Methods** The data were drawn from the Survey of Pathways to Diagnosis and Services (Pathways), a nationally representative survey conducted by the National Center for Health Statistics (NCHS), Centers of Disease Control, and Prevention (CDC) in 2011. Analysis of variance and chi square analysis were used to test for significant differences between groups comprised of children with ASD; ASD + ID, ASD + ADHD, and ASD + ADHD + ID.

**Results** In a population of children diagnosed with ASD, the rate of ADHD + ASD was 42% and the rate of ADHD + ASD + ID was 17%, resulting in a 59% total comorbidity rate of ADHD and ASD. Statistically significant differences in age when parents first wondered about problems with development, age when medical assistance was first sought, and age of reported ASD diagnosis were found between the ASD + ADHD and all other groups, with the ASD + ADHD being older. Average age at diagnosis was over 6 years for children with ASD + ADHD but close to 2.5 years for children with ASD only.

**Conclusions** The study of a nationally representative sample helps to elucidate prevalence rates but also raises questions about early identification and diagnosis when symptoms of both disorders are present. The findings point to the need for future research to understand why comorbidity is associated with delays in the age when medical assistance is sought.

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Res Dev Disabil. 2016 Aug;55:55-63.

**ADHD SUBTYPES AND NEUROPSYCHOLOGICAL PERFORMANCE IN AN ADULT SAMPLE.**

**Dobson-Patterson R, O’Gorman JG, Chan RCK, et al.**

The study investigated, with an adult sample, the hypothesis that differences between subtypes of ADHD on neuropsychological tests contribute to the poor separation of ADHD and healthy groups on tests of this kind. Groups of ADHD inattentive (n = 16) and combined (n = 16) subtypes were carefully identified using DSM-IV criteria, and their performance on 14 measures of attention, memory, and executive function (EF) was compared between subtypes and between the two subtypes combined and a group of healthy controls (n = 30). Multivariate analyses showed statistically significant differences between the two subtypes, and between the two subtypes combined and the healthy controls. Importantly for the hypothesis, where differences for neuropsychological tests in terms of effect sizes between subtypes were largest, the differences in effect sizes between the two groups combined and controls were smallest (r = -0.64, 95% CI [-0.15, -0.87]).

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Res Dev Disabil. 2016;59:93-104.

**DIFFERENTIAL IMPACT OF A MULTIMODAL VERSUS PHARMACOLOGICAL THERAPY ON THE CORE SYMPTOMS OF ATTENTION DEFICIT/HYPERACTIVITY DISORDER IN CHILDHOOD.**

**Amado L, Jarque S, Ceccato R.**

The aim of this study was to analyze the relative and differential efficacy of a combined versus medical treatment to reduce the symptoms of ADHD children in the school and family environment. A total of 100 subjects participated: 20 children with ADHD, their 40 parents and their 40 teachers. Half of the subjects were assigned to the drug group and half to the combined (drug plus psychosocial, psychoeducational intervention with teachers and mothers/fathers). Results The group analyses indicated that both treatments were effective, without significant differences between them. Individualized clinical analyses indicated that higher percentages of improvement and normalization were obtained in the children in the combined group than in the drug only group. Our findings point to the desirability of implementing long-lasting multimodal, multicontextual interventions for ADHD in childhood.

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Rev Neurol. 2016;63:71-78.

**THE NEUROANATOMY OF ATTENTION DEFICIT HYPERACTIVITY DISORDER: NEUROPSYCHOLOGICAL AND CLINICAL CORRELATES.**

**Albert J, Fernandez-Jaen A, Martin Fernandez-Mayoralas DM, et al.**

Introduction. The development of structural magnetic resonance scanning and new methods of analysis has made it possible to explore, in a hitherto unknown way, the neuroanatomical bases of attention deficit hyperactivity disorder (ADHD). Yet, little is known about the relation between the clinical symptoms and the neuropsychological dysfunctions characterising ADHD and the neuroanatomical alterations that are observed. Aim. To explore the relation between neuroanatomy, clinical features and neuropsychology in ADHD. Development. At group level, there are a number of marked differences between the brain of children, adolescents and adults with ADHD and the brain of subjects with a typical development. These differences are observed cross-sectionally and longitudinally in all the measurements, both in the grey matter and in the white matter. Although still scarce, there is an increasing body of evidence showing that these differences are related with the core symptoms of the disorder and with the degree of clinical dysfunction. They also appear to be associated with cognitive functioning (mainly attention and inhibitory control). Conclusions. The relation among the different levels of analysis in the study of ADHD bring research closer to the clinical features and allows a better understanding and management of the disorder. Although progress is undoubtedly being made in this field, there are still many questions that need exploring in greater depth. There is a need for a better understanding of the association between the neuroanatomical measurements and each dimension of the symptoms, and their relationship with other neuropsychological processes that are also involved in the disorder.

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Scand J Public Health. 2016 Feb;44:18-26.

**MENTAL PROBLEMS AND THEIR SOCIO-DEMOGRAPHIC DETERMINANTS IN YOUNG SCHOOLCHILDREN IN SWEDEN, A COUNTRY WITH HIGH GENDER AND INCOME EQUALITY.**

**Stenmark H, Bergstrom E, Hagglof B, et al.**

**AIMS:** Mental problems and their potential socio-demographic determinants were investigated in young schoolchildren in Sweden, a high-income country in the top of income- and gender-equality rankings.

**METHODS:** Cross-sectional study of 1465 schoolchildren in grades 3 and 6. Mental health was measured by the Child Behavior Checklist and the Youth Self Report (Total problems and 14 specific problem areas). Potential socio-demographic determinants were sex, parental education and occupation, family structure, and immigrant status.

**RESULTS:** Mental problems were present in 14% of the sixth graders and in 7% of the third graders. In grade 3, the mean total problem score was lower in girls than in boys, but the prevalence of problems at a subclinical/clinical level did not differ by sex. Furthermore, in nine to 13 of the 14 specific problem areas,

problems were equally distributed by sex, parental education, parental occupation, immigrant status, and family structure. In grade 6, both the total mean score and the overall odds of subclinical/clinical problems were similar in girls and boys. Likewise, in all the specific problem areas, problems were evenly distributed by parental education and occupation, and only independently associated with immigrant status and family structure in one problem area. In five specific problem areas, boys had higher odds of problems than girls.

**CONCLUSIONS:** This study shows that also in a relatively wealthy and equal country such as Sweden, mental problems are a significant child public health issue. The association between socio-demographic background and mental problems seems to be rather weak, but differ dependent on the type of mental problem in focus.

Seizure. 2016;40:108-13.

**UNDERSTANDING SLEEP PROBLEMS IN CHILDREN WITH EPILEPSY: ASSOCIATIONS WITH QUALITY OF LIFE, ATTENTION-DEFICIT HYPERACTIVITY DISORDER AND MATERNAL EMOTIONAL SYMPTOMS.**

**Ekinci O, Isik U, Gunes S, et al.**

**Purpose** This study aimed to (1) compare sleep problems between children and adolescents with epilepsy and non-epileptic controls, and (2) examine whether there is an association between sleep problems and quality of life, Attention-Deficit Hyperactivity Disorder (ADHD) and mothers' emotional symptoms. **Method** Fifty-three patients from a cohort of epilepsy (aged 7-18 years) and 28 controls with minor medical problems (aged 7-18 years) were included. Parents completed Children's Sleep Habits Questionnaire (CSHQ) and Kinder Lebensqualitätsfragebogen: Children's Quality of Life Questionnaire-revised (KINDL-R) for patients and controls. Turgay DSM-IV Disruptive Behavior Disorders Rating Scale (T-DSM-IV-S) parent and teacher forms were used to assess ADHD symptoms for patients. Mothers of the patients completed Beck Depression Inventory and State-Trait Anxiety Inventory (STAI). Neurology clinic charts were reviewed for the epilepsy-related variables. **Results** Children with epilepsy had a higher CSHQ Total score than the control group. Those with a CSHQ score >56 (which indicates moderate to severe sleep problems) had lower scores on KINDL-R. Parent-rated T-DSM-IV-S Total and Hyperactivity-Impulsivity scores, STAI trait and Beck scores were found to be higher in those with a CSHQ score >56. Significant positive correlations were found between CSHQ Total score and T-DSM-IV-S, STAI trait and Beck scores. Binary logistic regression analysis revealed that T-DSM-IV-S Total, Inattention and Hyperactivity-Impulsivity scores were significantly associated with a higher CSHQ Total score. None of the epilepsy-related variables were found to be related with the CSHQ Total score. **Conclusion** Among children with epilepsy, sleep problems lead to a poor quality of life. The link between sleep problems and psychiatric symptoms must be conceptualized as a bilateral relationship. ADHD appears to be the strongest predictor of sleep problems.

Sensors (Basel). 2016;16.

**QUANTITATIVE EVALUATION SYSTEM OF SOFT NEUROLOGICAL SIGNS FOR CHILDREN WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER.**

**Kaneko M, Yamashita Y, Iramina K.**

Attention deficit hyperactivity disorder (ADHD) is a neurodevelopmental disorder characterized by symptoms of inattention, hyperactivity, and impulsivity. Soft neurological signs (SNS) are minor neurological abnormalities in motor performance, and are used as one evaluation method for neurodevelopmental delays in children with ADHD. Our aim is to establish a quantitative evaluation system for children with ADHD. We focused on the arm movement called pronation and supination, which is one such soft neurological sign. Thirty three children with ADHD aged 7-11 years (27 males, six females) and twenty five adults participants aged 21-29 years old (19 males, six females) participated in our experiments. Our results suggested that the pronation and supination function in children with ADHD has a tendency to lag behind that of typically developing children by several years. From these results, our system has a possibility to objectively evaluate the neurodevelopmental delay of children with ADHD



Shiraz E Medical Journal. 2016;17.

**THE EFFECTIVENESS OF PARENT MANAGEMENT TRAINING (PMT) ON ANXIETY AND DEPRESSION IN PARENTS OF CHILDREN WITH ADHD.**

**Firouzkouhi Moghaddam M, Forouzan Nia R, Rakhshani T, et al.**

**Background:** Attention deficit hyperactivity disorder is one of the most common psychiatric problems in childhood and adolescence.

**Objectives:** The aim of this study is to evaluate the effectiveness of parent management training (PMT) and a positive parenting program on children's behavioral problems and parents' anxiety and depression reduction.

**Patients and Methods:** In this semi-experimental study, which was conducted in Zahedan 2011, 36 parents of ADHD children whose kids had been on medications from at least 8 weeks before the study participated. Data were collected by Conners questionnaires for parents and DASS questionnaires about anxiety and depression. We used paired t-tests, chi-square statistical procedures, and SPSS version 16 software for data analysis. The  $P < 0.05$  was considered significant.

**Results:** The mean Conners parents scale in the case group was (104.7 - 11.04) before and (92.4 - 8.72) after intervention. In the control group, it was (102.3-|22.38) before and (102.2-|19.94) after the intervention. The Conners scale changes in the case group before and after intervention was statistically significant ( $P$ -value = 0.0001) and in the control group there was no significant change in the Conners scale ( $P = 0.945$ ).

**Conclusions:** In general, this study showed that the parent behavioral management training could reduce ADHD symptoms in preschool children. One of the limitations of this study was the number of cases; therefore, a further survey with a larger group might be considered.

Tehran University Medical Journal. 2016;74:190-98.

**COMPARISON OF DULOXETINE AND METHYLPHENIDATE IN THE TREATMENT OF CHILDREN WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.**

**Dodangi N, Habibi N.**

**Background:** Attention-deficit/hyperactivity disorder (ADHD) is a common and mostly chronic mental health condition that affects children, adolescents, and adults. Stimulants and atomoxetine are first-line agents for the treatment of ADHD. Despite the impressive track record of stimulants in the treatment of ADHD, they fail in 25% of patients due to lack of efficacy or the emergence of unwanted side effects. Accordingly, this study carried out to compare efficacy and safety of duloxetine (a serotonin and norepinephrine reuptake inhibitor) and methylphenidate (a short acting stimulant) in the treatment of children with attention-deficit/hyperactivity disorder.

**Methods:** Twenty-four children diagnosed with ADHD participated in this 6 weeks open clinical trial. Patients were between 6 to 11 years old that had been referred to psychiatry clinic at Akhavan and Rofide Medical and Rehabilitation Center in Tehran from September 2012 to July 2014. Diagnosis was made by two child psychiatrist according to DSM- IV TR criteria. Thirteen patients received duloxetine and others received methylphenidate. Conner' parent rating scale-revised-short form (CPRS-RS) and ADHD-rating scale (ADHD-RS) were used at the beginning and then each two weeks to assess efficacy of treatment. Routine laboratory tests and electrocardiogram (ECG) was carried out in the beginning and end of the trial.

**Results:** Twenty children with ADHD completed the study (Ten in methylphenidate and ten in duloxetine group). In both groups, scales of CPRS-RS and ADHD-RS were reduced from baseline to endpoint, but this reduction in methylphenidate group was significantly greater than duloxetine group ( $P = 0.000$ ). The most common side effect was gastrointestinal problems in duloxetine group and anorexia in methylphenidate group. No serious side effects and no changes in laboratory and ECG indexes were seen in both groups.

**Conclusion:** Duloxetine is not efficacious as well as methylphenidate in treatment of children with ADHD. Although more research are needed to achieve more accurate results.

Terapia Psicológica. 2016;34:41-52.

**DEVELOPMENT OF A SELF REPORTED SCALE FOR ADHD IN CHILDHOOD (EA-ADHD): DELPHI STUDY AND PRELIMINARY PSYCHOMETRIC DATA.**

**Nicolás SS, Iraurgi I.**

The purpose of this study is to develop a self reported scale specifically designed to assess ADHD symptoms and signs (EA-TDAH).

**Methods:** A preliminary scale was generated based on DSM-IV criteria for ADHD and related signs. The Delphi technique was used due to analyze content and apparent validity. A pilot study was conducted using a normative sample compound by 382 children and adolescents aged nine to 17. The EA-TDAH scale was rated by experts as clinically useful, and it showed high internal consistency ( $\alpha=.86$ ) and an adequate structural validity with two components. According to YSR's DSM correspondences, participants were classified as possible ADHD cases (13.8%) and not ADHD cases, it was the first group that showed higher ratings in the new scale. Although further investigation with clinical samples is needed, EA-TDAH seems to be an adequate scale for assessing ADHD symptoms and signs.

Trials. 2016;17.

**MELATONIN IN YOUTH: N-OF-1 TRIALS IN A STIMULANT-TREATED ADHD POPULATION (MYNAP): STUDY PROTOCOL FOR A RANDOMIZED CONTROLLED TRIAL.**

**Punja S, Nikles CJ, Senior H, et al.**

**Background:** Attention-deficit/hyperactivity disorder (ADHD) is a common neurological disorder affecting 5 % of children worldwide. A prevalent problem for children with ADHD is initial insomnia. The gold standard treatment to manage ADHD symptoms is stimulant medications, which may exacerbate the severity of existing initial insomnia. Currently, no gold standard treatment option exists for initial insomnia for these children. Melatonin, a hormone and a popular natural health product, is commonly provided to children by parents and recommended by healthcare providers, but high quality pediatric evidence is lacking.

**Methods/design:** This trial is a multicenter randomized triple-blind, placebo-controlled, parallel-group, randomized, controlled trial (RCT), in which each participant is offered an N-of-1 trial. An N-of-1 trial is a multiple-crossover, randomized, controlled trial conducted in a single individual. For the N-of-1 trial, each participant will undergo three pairs of treatment/placebo periods; each period is 1 week in length. Half the participants will have melatonin in the first period, the other half will start with placebo, and this will make up the parallel-group RCT. The primary outcome will be mean difference in sleep onset latency as measured by sleep diaries. A comparison of treatment effects yielded by the RCT data versus the aggregated N-of-1 trial data will also be assessed.

**Discussion:** This trial will provide rigorous evidence for the effectiveness of melatonin in children with ADHD on stimulants who experience initial insomnia. Further, this study will provide the first prospectively planned head-to-head comparison of RCT data with pooled data from a series of N-of-1 trials. Aggregated N-of-1 trials may be a powerful tool to produce high quality clinical trial evidence.

**Trial registration numbers:** ClinicalTrials.gov, NCT02333149. Registered on 16 December 2014. Australian New Zealand Clinical Trials Registry, ACTRN12614000542695. Registered on 21 May 2014.

Z Kinder Jugendpsychiatr Psychother. 2016;44:127-37.

**WISC-IV PERFORMANCES OF YOUNG MALE SUBJECTS WITH AD(H)D, THE BENEFITS OF APPLYING COGNITIVE PROFILE ANALYSIS TO DIAGNOSTICS.**

**Walz M, Bowi U, El-Wahsch D.**

**OBJECTIVE:** Studies suggest that children and adolescents suffering from AD(H)D show a specific WISC-IV profile in comparison to subjects of the same age group without any mental disorder. The present study compares the cognitive profiles of male subjects with AD(H)D to those of a clinical control group. The benefits of applying an ADHD specific cognitive profile analysis to differential diagnostics are analyzed.

**METHOD:** The WISC-IV profiles of 50 male subjects with AD(H)D (8 to 15 years) were compared with the profiles of 54 male children and adolescents (7 to 16 years) with other mental disorders. In addition, subgroup differences within the AD(H)D group were investigated.

**RESULTS:** Subjects with AD(H)D showed a significant lower processing speed than the control group. Within the AD(H)D group, patients with ADD showed the lowest speed index. There were no group differences in total IQ and other WISC-IV indexes.

**CONCLUSIONS:** A WISC-IV profile analysis is not a suitable instrument to certainly confirm or exclude an AD(H)D diagnosis. Nevertheless, the results of the present study speak for considering the WISC-IV profile in the diagnosis of AD(H)D as it increases the sensitivity of the clinical diagnostic process and provides useful indicators for differential diagnosis.

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Z Kinder- Jugendpsychiatr Psychother. 2016;44:307-14.

**TRUST, BUT VERIFY. THE ERRORS AND MISINTERPRETATIONS IN THE COCHRANE ANALYSIS BY O.J. STOREBO AND COLLEAGUES ON THE EFFICACY AND SAFETY OF METHYLPHENIDATE FOR THE TREATMENT OF CHILDREN AND ADOLESCENTS WITH ADHD.**

**Banaschewski T, Gerlach M, Becker K, et al.**

**Objective:** A recent Cochrane review published by O. J. Storebo and colleagues (2015) raised substantial doubts about the benefit from stimulant medication with methylphenidate in the treatment of childhood ADHD due to the overall poor quality of studies. The systematic review thus contradicts all previous reviews and meta-analyses.

**Method:** We here detail various examples of errors, inconsistencies, and misinterpretations in the review which led to false results and inadequate conclusions.

**Results:** We demonstrate that the study selection is flawed and undertaken without sufficient scientific justification resulting in an underestimation of effect sizes, which, furthermore, are inadmissibly clinically interpreted. The methodology of the assessment of bias and quality is not objective and cannot be substantiated by the data.

**Conclusions:** Cochrane reviews lay claim to a high scientific quality and substantial relevance for evidence-based clinical decisions. The systematic review by Storebo and colleagues (2015) illustrates that, despite adhering to strict standards and high-quality protocols, even Cochrane works should be critically read and verified, sometimes with surprising results.

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# Association Between ADHD and Obesity: A Systematic Review and Meta-Analysis

Samuele Cortese, M.D., Ph.D., Carlos Renato Moreira-Maia, M.D., Ph.D., Diane St. Fleur, M.D., Carmen Morcillo-Peñalver, M.D., Luis Augusto Rohde, M.D., Ph.D., Stephen V. Faraone, Ph.D.

**Objective:** Impulsivity and inattention related to attention deficit hyperactivity disorder (ADHD) may increase food intake and, consequently, weight gain. However, findings on the association between obesity/overweight and ADHD are mixed. The authors conducted a meta-analysis to estimate this association.

**Method:** A broad range of databases was searched through Aug. 31, 2014. Unpublished studies were also obtained. Study quality was rated with the Newcastle-Ottawa Scale. Random-effects models were used.

**Results:** Forty-two studies that included a total of 728,136 individuals (48,161 ADHD subjects; 679,975 comparison subjects) were retained. A significant association between obesity and ADHD was found for both children (odds ratio=1.20, 95% CI=1.05–1.37) and adults (odds ratio=1.55, 95% CI=1.32–1.81). The pooled prevalence of obesity was increased by about 70% in adults with ADHD (28.2%, 95% CI=22.8–34.4) compared with those without ADHD (16.4%,

95% CI=13.4–19.9), and by about 40% in children with ADHD (10.3%, 95% CI=7.9–13.3) compared with those without ADHD (7.4%, 95% CI=5.4–10.1). The significant association between ADHD and obesity remained when limited to studies 1) reporting odds ratios adjusted for possible confounding factors; 2) diagnosing ADHD by direct interview; and 3) using directly measured height and weight. Gender, study setting, study country, and study quality did not moderate the association between obesity and ADHD. ADHD was also significantly associated with overweight. Individuals medicated for ADHD were not at higher risk of obesity.

**Conclusions:** This study provides meta-analytic evidence for a significant association between ADHD and obesity/overweight. Further research should address possible underlying mechanisms and the long-term effects of ADHD treatments on weight in individuals with both ADHD and obesity.

*Am J Psychiatry* 2016; 173:34–43; doi: 10.1176/appi.ajp.2015.15020266

Obesity is a major public health issue, affecting 17% of children and 35% of adults in the United States (1), and obesity is one of the main causes of morbidity and mortality (2). It has been estimated that obesity-related medical costs in the United States will rise to \$48 billion–\$66 billion per year by 2030 (2). Therefore, it is a public health priority to understand the factors that contribute to obesity in order to design evidence-based prevention strategies (3).

Attention deficit hyperactivity disorder (ADHD) is another frequent and impairing condition, with a worldwide prevalence estimated at about 5% in school-age children (4) and persistence of impairing symptoms in adulthood in up to 65% of cases (5). Average annual incremental costs of ADHD in the United States have been calculated at \$143 billion–\$266 billion (6).

A number of studies have reported a significant association between obesity and ADHD (e.g., see references 7–10), but others failed to confirm this finding (e.g., see references 11–13). The putative association between ADHD and obesity might seem paradoxical because, rather than being hyperactive, individuals

with obesity are often described as “lazy” (14). However, the impulsivity and inattention that characterize ADHD might lead to dysregulated eating patterns with consequent weight gain (15). The role of possible confounders, including low socioeconomic status and comorbid mental health conditions, in explaining the association between obesity and ADHD is still unclear (7, 9, 12, 16). In addition, the role of age, gender, study setting, or study country is also uncertain (9, 10, 12, 13, 17–19).

Establishing whether, and to what extent, obesity and ADHD are associated is highly relevant from a clinical and public health standpoint. Because obesity and ADHD are common conditions, should a significant association be found, individuals affected by both would represent a sizable portion of the general population in need of care. In addition, the finding of a significant association would prompt research on underlying causal mechanisms. Finally, the association might have relevant treatment implications. Indeed, preliminary evidence from a previous study showed that treating ADHD with psychostimulants reduced obesity in individuals with

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both conditions, possibly because of a sustained decrease in impulsivity and improvement in organizational skills (15).

Given the uncertainty about the association between ADHD and obesity, as well as the roles of socioeconomic status, psychiatric comorbidities, age, gender, and study setting/country, we conducted a systematic review and meta-analysis to estimate the association between obesity and ADHD. We hypothesized a significant association, even after taking into account the aforementioned factors. We performed an additional meta-analysis of studies reporting data on overweight because its association with ADHD is also unclear (11–13, 20–22). Finally, to gain insights into the effect of ADHD medications, we meta-analyzed informative studies.

## METHOD

We followed the recommendations of the Meta-Analysis of Observational Studies in Epidemiology group (23) and the Preferred Reporting Items for Systematic Reviews and Meta-Analyses statement (24). The protocol of the present meta-analysis has been published previously (25).

### Search Methods

We searched a broad range of electronic databases from inception to Aug. 31, 2014, and also gathered unpublished material. Further details are reported in Appendix A1 in the data supplement that accompanies the online edition of this article.

### Selection Criteria

*Study type.* We included studies that reported the degree of association, expressed as an odds ratio, between obesity and ADHD, or data for calculating the odds ratio. We considered 1) population-based studies and 2) clinical studies of individuals with ADHD compared with non-ADHD controls. We did not include studies of individuals in bariatric clinics because these individuals represent a subsample of severely obese individuals, whereas our meta-analysis focuses on the association between ADHD and any degree of obesity. For longitudinal studies, we extracted data at baseline or at the earliest time point.

*Population.* Individuals with ADHD were those who had 1) ADHD as defined by DSM or hyperkinetic disorder as defined by ICD (26); 2) scores above a symptom threshold on a validated ADHD rating scale; 3) a positive answer to the question “Did your doctor ever tell you that you have ADHD?”; or 4) a medical record diagnosis of ADHD. The presence of psychiatric comorbidities, which are often associated with ADHD (27), was not an exclusion criterion. We excluded studies where ADHD was comorbid with specific disorders affecting weight (e.g., Prader-Willi syndrome).

Comparison subjects were participants without ADHD.

*Outcomes.* The primary outcome measure was the odds ratio expressing the association between obesity and ADHD. Obesity was defined either by self-report or medical record diagnosis or by body mass index (BMI), derived from self-

reported or directly measured weight and height, above a preset value. In adults this value was a BMI  $\geq 30$ , as defined by the World Health Organization (28). In children there is no consensus on the definition of obesity (29). Whereas some authors have used BMI  $>95$ th,  $>97$ th, or  $>98$ th percentile for age and sex, others have relied on percentile curves that pass through the points of a BMI score of 30 (30). Therefore, we included all available definitions. Authors of studies reporting BMI or height and weight, but not obesity rates, were asked to provide obesity rates based on the following definitions: adults: BMI  $\geq 30$ ; children: BMI  $>95$ th percentile for age and sex.

The secondary outcome measure was the odds ratio expressing the association between ADHD and overweight, defined either by self-report or medical record diagnosis or by a BMI  $\geq 25$  in adults or  $>85$ th percentile in children (31), derived from self-reported or directly measured weight and height. Therefore, “overweight” included “obesity.”

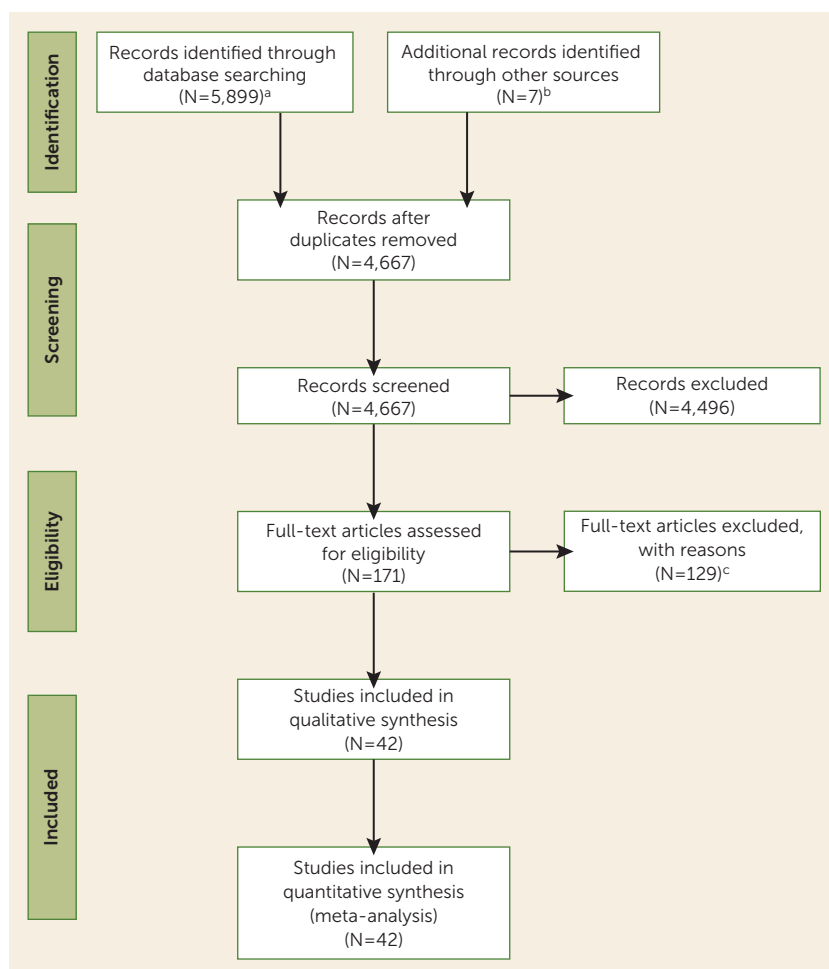
### Selection of Studies, Data Extraction, and Assessment of Study Quality

These steps were performed blindly by S.C. and C.R.M.M., as detailed in Appendix A1 in the online data supplement. Study quality was rated using the Newcastle-Ottawa Scale (32), as recommended by the Cochrane collaboration (33) (see Appendix A2 in the data supplement).

### Statistical Analysis

Odds ratios were extracted when available or calculated from available data. Meta-analyses used random-effects models. We chose a random-effects model because it allows the true population effect size to differ among studies. First, we meta-analyzed unadjusted odds ratios across all studies. We then conducted subgroup meta-analyses of studies 1) of children and adolescents (because of a paucity of data, it was not possible to separately analyze children and adolescents); 2) of adults; 3) using a formal diagnosis of ADHD; that is, based on a psychiatric interview addressing DSM or ICD criteria; 4) where obesity was defined based on directly measured height and weight; 5) of population-based samples; and 6) of clinical samples. To represent the highest quality studies, we pooled studies with both a formal ADHD diagnosis and direct measures of height and weight. We then meta-analyzed adjusted odds ratios. The confounders adjusted for included psychiatric comorbidities, such as depression, and socioeconomic status; these varied across studies (see Table S1 in the data supplement). Additionally, we performed meta-regression analyses including unadjusted odds ratios as outcome and year of study publication, number of participants with and without ADHD, age group (children/adolescents, adults), gender, study setting (clinical, population-based), study country, and the rating on the Newcastle-Ottawa Scale as regressors. For the outcome “overweight,” we performed only a meta-analysis of unadjusted odds ratios because there were insufficient data for other analyses. We also performed meta-analyses in medicated and unmedicated subjects, selecting studies that reported both data in medicated and nonmedicated individuals.



**FIGURE 1. Flow Diagram of Study Selection, as Specified by the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) Statement**

<sup>a</sup> Results for each electronic database are reported in Appendix A1 in the online data supplement.

<sup>b</sup> These refer to three unpublished studies (36–38) plus four studies (9, 11, 47, 50) that were unpublished when the search was first conducted and were subsequently published; all seven studies were included in the meta-analysis.

<sup>c</sup> References of excluded studies are reported, with reasons for exclusion, in Table S3 in the data supplement.

The meta-analyses and meta-analytic regressions were weighted by the reciprocal of the variance of the effect size, which gives greater weight to larger studies (34). We used the  $I^2$  index to assess the heterogeneity of effect sizes. The  $I^2$  index estimates the percentage of variation among effect sizes that can be attributed to heterogeneity. A significant  $I^2$  indicates that the degree of heterogeneity is greater than would be expected by chance. We used Egger's test (35) to assess publication biases.

Finally, we calculated the pooled prevalence of obesity in participants with and without ADHD, and in subjects medicated and nonmedicated for ADHD, using random-effects models. Analyses were performed using STATA 13.1 (SAS Institute, Cary, N.C.) and Comprehensive Meta-Analysis (<http://www.meta-analysis.com/index.php>).

## RESULTS

Figure 1 shows the study selection process. We retained 42 studies (7–13, 16–18, 20–22, 36–64) for the meta-analysis,

comprising 728,136 participants: 48,161 with ADHD (46,115 children; 2,046 adults) and 679,975 comparison subjects (616,228 children; 63,747 adults) (see Table S2 in the online data supplement). One study (51) presented data only for overweight rather than for obesity. Studies not included in the meta-analysis after assessment of the full text are listed, with reasons for exclusion, in Table S3 in the data supplement.

The results of all analyses are summarized in Table 1, which reports tests of heterogeneity and publication bias (Egger's test). Our first analysis of all available studies (N=41) reporting unadjusted odds ratios for obesity found a significant pooled odds ratio for obesity in individuals with ADHD compared with controls (odds ratio=1.30, 95% CI=1.16–1.46) (Figure 2). Heterogeneity was high and significant, while Egger's test was not significant. After removing one clear outlier (8), results remained significant (odds ratio=1.3, 95% CI=1.1–1.4). Because four studies (43, 45, 59, 64) used unscreened population-based control groups, which may have included individuals

with ADHD, we repeated the analysis without these studies. Results were unchanged (odds ratio=1.3, 95% CI=1.1–1.4).

In both analyses limited to children/adolescents and adults, the pooled odds ratios were significant (odds ratio=1.20, 95% CI=1.05–1.37; and odds ratio=1.55, 95% CI=1.32–1.81, respectively; for further details, see Appendix A3 and Figures S1–S2 in the online data supplement).

The pooled prevalence of obesity was increased by about 70% in adults with ADHD (28.2%, 95% CI=22.8–34.4) compared with adults without ADHD (16.4%, 95% CI=13.4–19.9) and by about 40% in children with ADHD (10.3%, 95% CI=7.9–13.3) compared with children without ADHD (7.4%, 95% CI=5.4–10.1).

Subgroup meta-analyses of studies 1) using a formal diagnosis of ADHD (odds ratio=1.36, 95% CI=1.12–1.66, Figure S3 in the data supplement); 2) with measured height and weight (odds ratio=1.32, 95% CI=1.06–1.66, Figure S4 in the data supplement); 3) in population-based samples (odds ratio=1.24, 95% CI=1.10–1.39, Figure S5 in the data supplement);

**TABLE 1. Summary of Results Showing Pooled Odds Ratios in the Main Meta-Analysis and in the Subgroup Meta-Analyses**

Outcome	Type of Analysis	N Studies	Odds Ratio	95% CI	p	Heterogeneity			Egger's Test (Publication Bias)	
						$\chi^2$	p	$I^2$	t	p
Obesity	All available studies	41	1.30	1.16–1.46	<0.0005	197.22	<0.0005	79.7	1.78	0.083
Obesity	Limited to children/adolescents	30	1.20	1.05–1.37	0.009	164.26	<0.0005	82.3	0.95	0.349
Obesity	Limited to adults	11	1.55	1.32–1.81	<0.0005	13.90	0.178	28.1	1.79	0.106
Obesity	Limited to studies with a formal diagnosis of ADHD	25	1.36	1.12–1.66	0.002	81.68	<0.0005	70.6	0.44	0.66
Obesity	Limited to studies using measured height and weight	24	1.32	1.06–1.66	0.015	110.81	<0.0005	79.2	2.44	0.023
Obesity	Limited to studies with a formal diagnosis of ADHD and measured height and weight	17	1.47	1.12–1.93	0.006	42.26	<0.0005	62.1	0.44	0.667
Obesity	Limited to population-based studies	26	1.24	1.10–1.39	0.001	146.77	<0.0005	83.0	1.01	0.320
Obesity	Limited to clinical studies	15	1.61	1.10–2.35	0.015	43.82	<0.0005	68.1	0.86	0.407
Obesity	Limited to studies reporting adjusted odds ratios	16	1.27	1.11–1.44	<0.0005	24.69	0.054	39.3	2.09	0.056
Overweight (including obesity)	All available studies	22	1.17	1.01–1.36	0.042	94.69	<0.0005	77.8	2.44	0.024
Obesity	Limited to unmedicated participants	12	1.43	1.23–1.67	<0.0005	21.15	0.032	48.0	–0.29	0.781
Obesity	Limited to medicated participants	12	1.00	0.87–1.15	0.964	22.89	0.018	51.9	–1.73	0.115

and 4) in clinical samples (odds ratio=1.61, 95% CI=1.10–2.35, Figure S6 in the data supplement) each found a statistically significant pooled odds ratio (see Appendix A3 in the data supplement). The meta-analysis limited to studies with a formal diagnosis of ADHD and direct measures of height and weight confirmed a significant association between ADHD and obesity (odds ratio=1.47, 95% CI=1.12–1.93, see Figure S7 and Appendix A3 in the data supplement).

The meta-analysis of adjusted odds ratios found a statistically significant pooled odds ratio (odds ratio=1.27, 95% CI=1.11–1.44, Figure 3). The heterogeneity and publication bias statistics were not significant.

Meta-regression analysis showed that year of study publication, number of participants with and without ADHD, age group, gender, study setting, and rating on the Newcastle-Ottawa Scale did not significantly influence the pooled odds ratios. The effect of study country, based on a total of 17 countries, was shy of statistical significance ( $p=0.0506$ ) (see Appendix A3 in the online data supplement).

The meta-analysis of odds ratios for overweight (22 studies) found a statistically significant pooled odds ratio (odds ratio=1.17, 95% CI=1.01–1.36, Figure S8 in the data supplement); heterogeneity was high and significant, while Egger's test was not significant.

Data on both medicated and nonmedicated participants with ADHD were available from 12 studies. The association between ADHD and obesity was significant for unmedicated (odds ratio=1.43, 95% CI=1.23–1.67, Figure 4A) but not for medicated (odds ratio=1.00, 95% CI=0.87–1.15, Figure 4B) individuals with ADHD. Further details are reported in Appendix A3 in the data supplement.

The pooled prevalence of obesity in participants medicated for ADHD (13.8%, 95% CI=11.4–16.6) was decreased by

about 40% compared with those not medicated (19.2%, 95% CI=16.1–22.7).

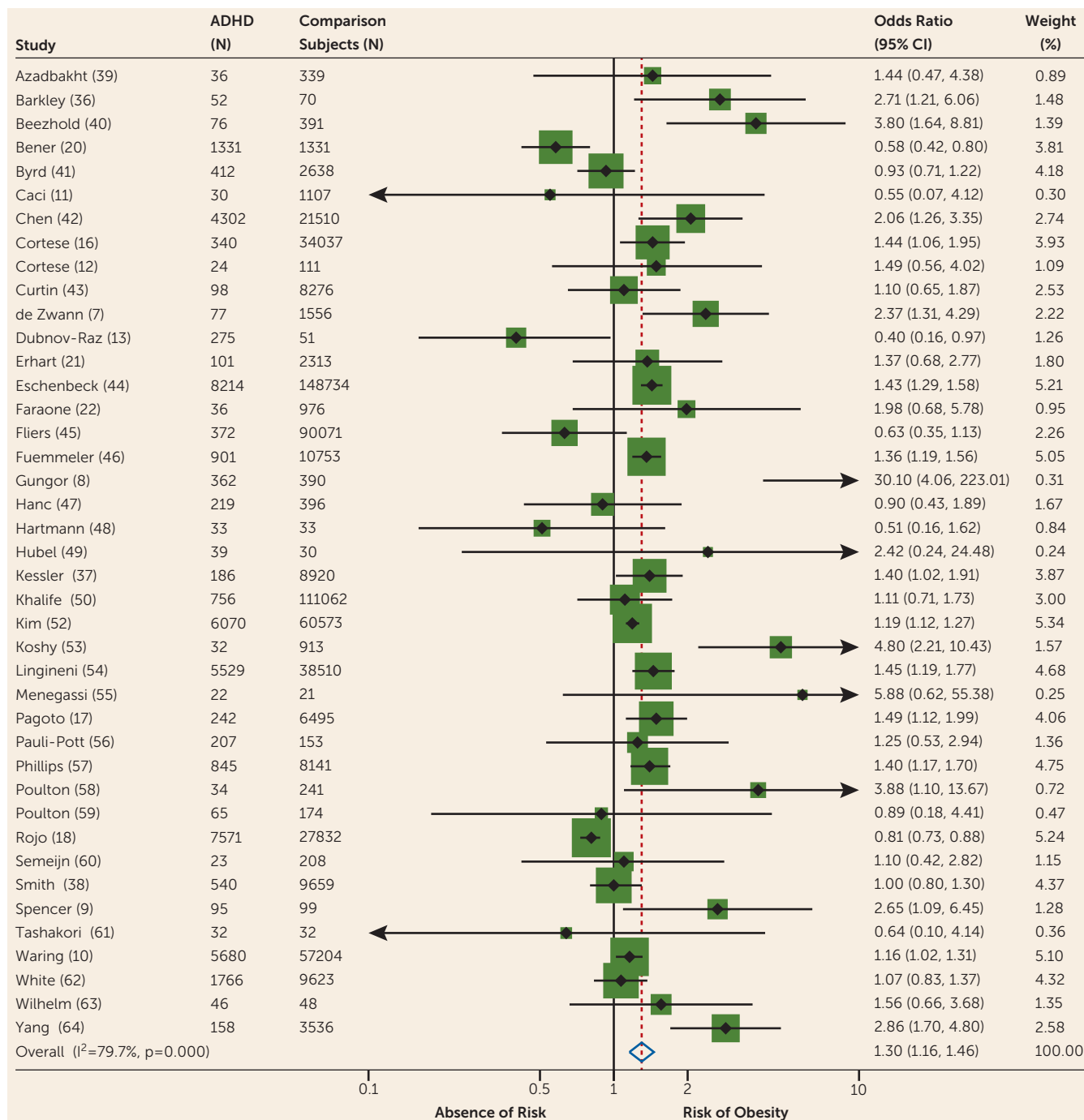
## DISCUSSION

To our knowledge, this is the first meta-analysis assessing the relationship between ADHD and obesity. We found a statistically significant association between these two conditions. The pooled prevalence of obesity was increased by about 70% in adults with ADHD and 40% in children with ADHD compared with subjects without ADHD. These figures, considering the high prevalence of ADHD and the impairment associated with obesity, translate into a conspicuous burden for society.

A significant association emerged also when pooling odds ratios adjusted for possible confounders, including socioeconomic status and comorbid psychiatric conditions (65). This conclusion should be considered with caution because the type and number of factors adjusted for varied across studies; future research should systematically adjust for a broad set of possible confounders. Special attention should be given to common ADHD comorbid conditions, such as depression, that are also associated with obesity.

Using subgroup meta-analyses, we clarified the role of other factors. We found that the significant association between obesity and ADHD persisted even when focusing only on studies with a formal diagnosis of ADHD, making it unlikely that our results were biased by nonoptimal procedures to detect ADHD, in particular self-reported diagnoses. Another subgroup meta-analysis showed that results did not substantially change when considering only obesity values calculated from directly measured height and weight, suggesting that lower-quality procedures for measuring obesity did not bias our results.

**FIGURE 2. Unadjusted Odds Ratios Expressing the Association Between Obesity and ADHD<sup>a</sup>**

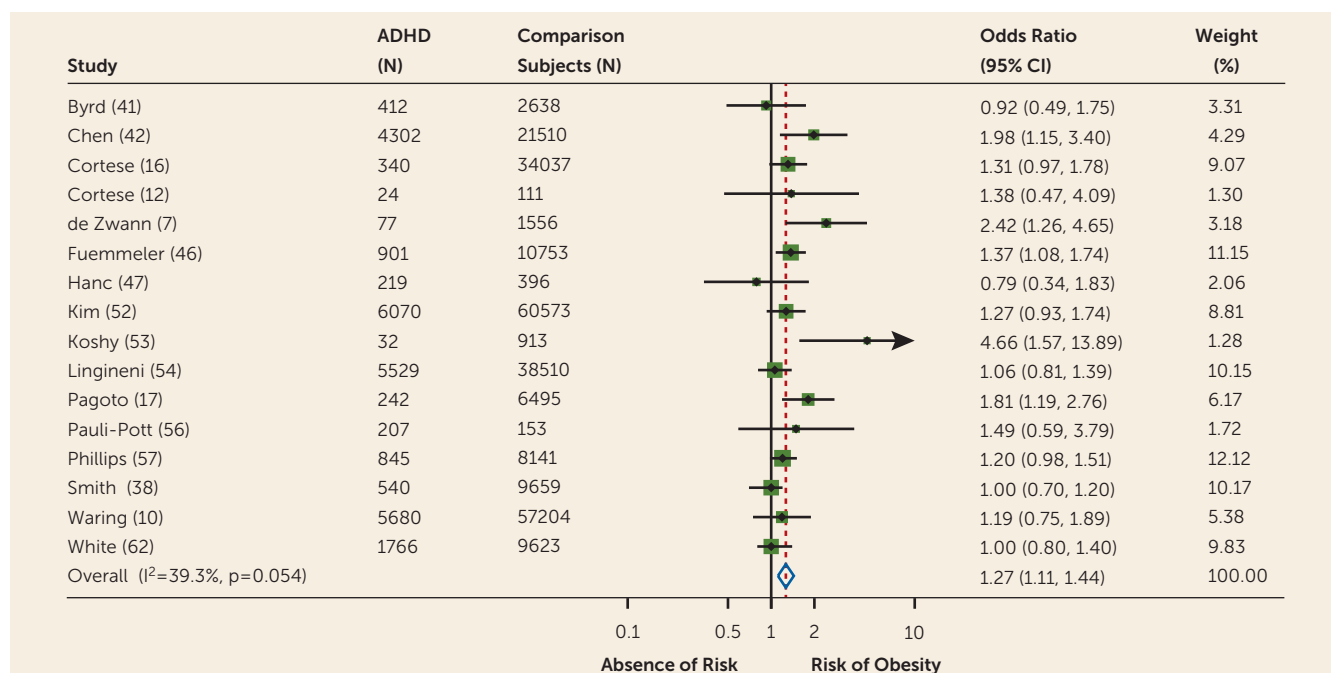


<sup>a</sup> The area of each square is proportional to the weight that the individual study contributed to the meta-analysis. Weights are from random-effects analysis.

Our meta-regression analysis shed light on the role of additional factors. Prior work has suggested that the association between ADHD and obesity is influenced by gender. One study (19) of children and adolescents reported a significant association between ADHD symptoms and obesity only in adolescent females; two other studies (41, 52) found higher odds ratios in unmedicated female adolescents than in male adolescents. According to some authors (52), higher

rates of binge eating in females may mediate this gender effect. But, in contrast to these scattered findings, we showed that gender did not significantly affect the association between ADHD and obesity.

We also found that age group (children/adolescents versus adults) did not influence the association between ADHD and obesity, suggesting that the relationship is already present in childhood. Because only three studies (43–45) presented data

FIGURE 3. Adjusted Odds Ratios Expressing the Association Between Obesity and ADHD<sup>a</sup>

<sup>a</sup> The area of each square is proportional to the weight that the individual study contributed to the meta-analysis. Weights are from random-effects analysis.

in children and adolescents separately (for details, see Appendix A4 in the online data supplement), we could not compare odds ratios in these two developmental periods. It is possible that the significant association between ADHD and obesity in the children/adolescents group was driven either by the primary school group or by the adolescent group. Therefore, further research focusing separately on these two age groups is warranted.

Consistent with our meta-regression analysis, our subgroup analysis showed that the association between obesity and ADHD was similar in clinical and population-based samples; therefore, putative clinical referral biases cannot account for the association.

The effect of study country failed to reach statistical significance. This conclusion should be considered with caution because for the majority of countries only one or two studies were available. Finally, study quality was not a significant predictor in the meta-regression analyses, which is consistent with our subgroup meta-analysis showing the persistence of significant results when including only the most rigorous studies; that is, those with a formal ADHD diagnosis and in which height and weight were measured directly. It is also noteworthy that publication bias was not significant in the majority of the meta-analyses performed.

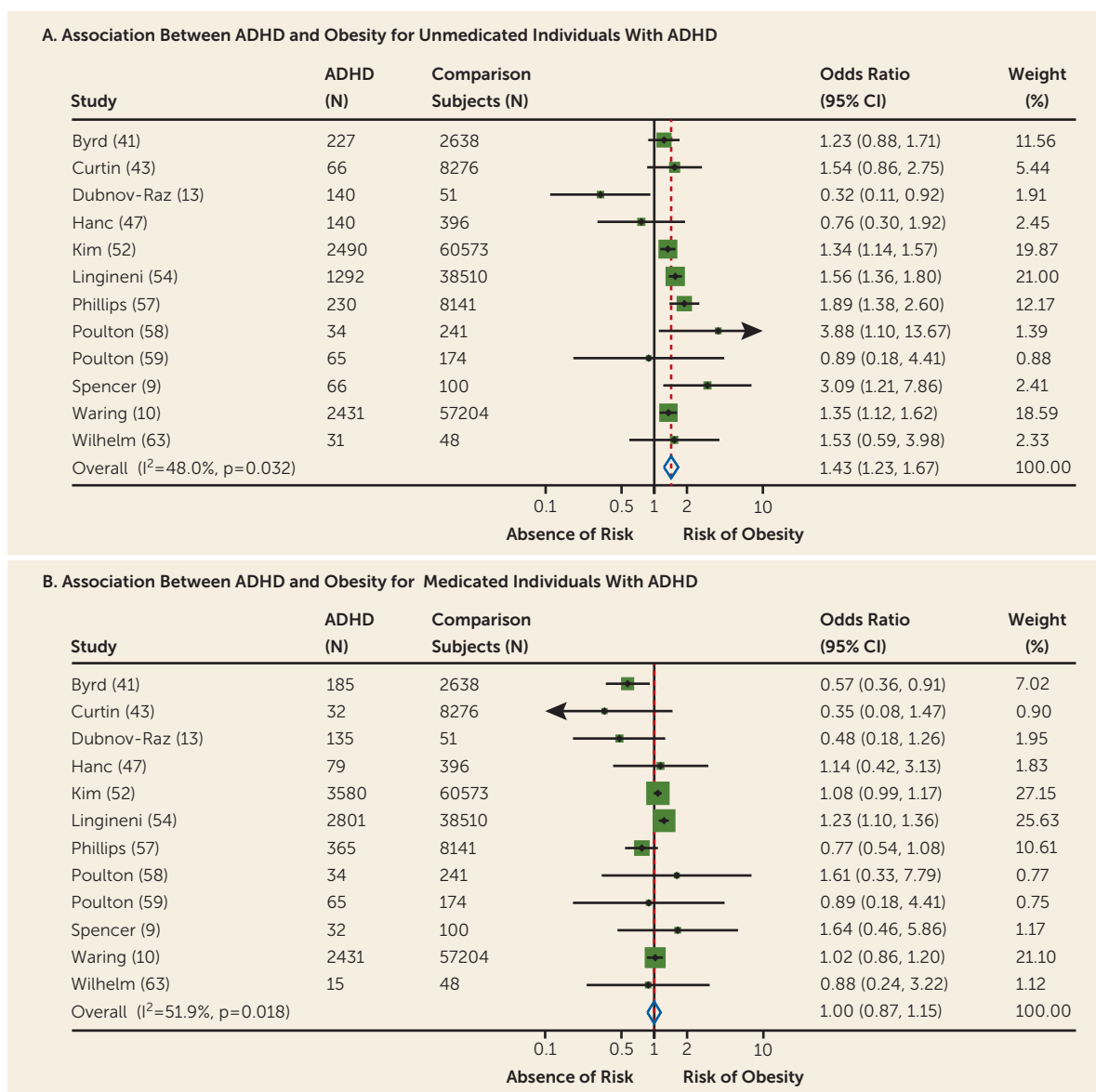
We also found a significant association between ADHD and overweight, suggesting that future research in the field should examine less severe grades of weight excess in addition to obesity.

In the analyses focused on medication status, we found a nonsignificant association in individuals pharmacologically treated for ADHD, who had rates of obesity that were decreased by about 40% compared with those not treated.

These results should be considered with caution because they are based on a subset of studies ( $N=12$ ), although the total number of participants was still high (9,754 medicated individuals with ADHD; 7,212 nonmedicated individuals with ADHD; 176,352 individuals without ADHD). Importantly, our results based on correlational studies cannot prove that pharmacological treatment for ADHD decreases the risk of obesity associated with ADHD. Overall, there is limited empirical evidence on the short- and long-term effects of psychostimulants on weight specifically focusing on individuals with ADHD and obesity. We are aware of only one naturalistic study (66) showing that treating comorbid ADHD in adults with a lengthy history of unsuccessful weight loss significantly improved weight loss at 15 months. In that study, appetite suppression vanished within 2 months after the start of the treatment. The study authors argue that the temporary anorexigenic effect of psychostimulants could not account for the observed improvement. Rather, it is possible that the improvements in executive functioning and decreased impulsivity led to more regular eating patterns, with consequent better adherence to diet. Given the scant available research, our results should prompt further investigation on the short- and long-term effects of psychostimulants on weight, aimed at establishing whether weight reduction is causally related to direct metabolic effects of psychostimulants, to long-term normalization of eating patterns, or to other indirect mechanisms. The effects on obesity of nonpharmacological treatments for ADHD should be systematically investigated as well.

The cross-sectional data that we analyzed do not permit firm conclusions about causality in the association between ADHD and obesity. Preliminary longitudinal evidence

**FIGURE 4. Forest Plot Showing the Results of the Subgroup Meta-Analyses of Studies Including Nonmedicated Participants With ADHD Only and Medicated Participants With ADHD Only<sup>a</sup>**



<sup>a</sup>The area of each square is proportional to the weight that the individual study contributed to the meta-analysis. Weights are from random-effects analysis.

suggests that ADHD may temporarily precede, and thus contribute to, obesity. A prospective study of 8,106 children (50) concluded that childhood ADHD symptoms predicted subsequent obesity, rather than the opposite. Another longitudinal study (12) found that men with a childhood diagnosis of ADHD had a twofold higher rate of obesity compared with those without such a diagnosis. However, because anthropometric data at baseline were not available, the results of that study are equivocal.

Lacking a clear signal from longitudinal studies, several possibilities arise: 1) ADHD could increase the risk of obesity; 2) ADHD and obesity share common biological risk factors, including genetic variants (67, 68); and 3) obesity or factors associated with it cause or mimic ADHD.

With regard to the first hypothesis, both the impulsive and inattentive components of ADHD could increase the risk of obesity (15). Deficient inhibitory control, which is an expression of impulsivity and characterizes a large subgroup of individuals with ADHD, could reinforce abnormal eating behaviors that, in turn, would increase the likelihood of obesity (15). Inattention and poor planning might cause difficulties in adhering to regular eating patterns and dietary regimens (15); additionally, lack of attention may be associated with lack of awareness of food intake. The hyperactive component of ADHD, as motor overactivity, would intuitively be considered to decrease, rather than increase, the risk of obesity, assuming that it increases energy expenditure and weight loss. However, ADHD motor hyperactivity is not constant but is modulated by the context. For



example, it decreases while watching television (69), and children with ADHD have been shown to watch more television and engage in less physical activity than comparison subjects without ADHD (52). In addition, hyperactivity linked to restless behaviors may also include abnormal eating patterns. Given the paucity of data, we could not assess the effect of ADHD subtypes, ADHD symptom severity or frequency, and other variables (e.g., watching television, sedentary activity) related to ADHD and obesity. These represent areas of future research for the field.

The hypothesis of common neurobiological dysfunctions in obesity and ADHD reflects the recent notion that many conditions classically thought to be nervous system disorders also include alterations in other physiological systems (70). ADHD and obesity may share dopaminergic dysfunctions underpinning reward deficiency processing, but this understanding needs to be better evaluated (71). Interestingly, a “reward deficiency syndrome,” characterized by insufficient dopamine-related natural reinforcement that leads to “unnatural” immediate rewards (such as inappropriate eating), has been reported in both ADHD and obesity (71). In addition, oxidative stress, which is linked to obesity, has also been associated with ADHD (72). Moreover, treatment with omega-3 fatty acids, a potent antioxidant, yields significant, albeit modest, reductions in ADHD symptoms (73).

Finally, it is possible that factors associated with obesity lead to ADHD-like symptoms. Both sleep-disordered breathing (71) and shorter or later sleep have been reported to manifest with ADHD-like symptoms.

Our results have important clinical and public health implications. The obesity associated with ADHD might explain why patients with ADHD are at increased risk for higher cholesterol levels and higher blood pressure (9). Assessing the risk for obesity should be part of the assessment and management of ADHD. Clinicians should also screen for ADHD in individuals who are referred for obesity, especially those with a previous history of unsuccessful weight-loss attempts. Although obesity has been found to be associated with other mental health conditions, such as depression (74) and anxiety (75), its association with ADHD might be particularly significant for its potential treatment implications.

Our results should be considered in the context of some limitations. First, we endeavored to include unpublished studies, asking experts in the field to provide relevant data, but we could not contact all experts. The inclusion of data from unpublished studies can itself introduce bias due to the willingness of investigators of located unpublished studies to provide data (18). Second, the definition of obesity in studies in children was based on different BMI thresholds, reflecting a lack of consensus in the field. Third, the exclusion of studies in bariatric samples, although sound, may have led to an underestimation of the strength of the association between ADHD and obesity. Fourth, we focused on obesity/overweight, although a bimodal distribution of weight status in ADHD is possible, whereby ADHD is associated with both obesity/overweight and underweight. This should be assessed in future systematic reviews and meta-analyses.

Finally, although we aimed to reduce study heterogeneity by means of subgroup meta-analyses, heterogeneity was still significant in these subgroup analyses. However, in the analysis including studies with adjusted odds ratios, the degree of heterogeneity was not significant.

## CONCLUSIONS

We found meta-analytic evidence of a significant association between obesity/overweight and ADHD, regardless of possible confounders. Mediation effects and causal mechanisms underlying the association, as well as the long-term effects of ADHD medications on weight status in individuals with obesity and ADHD, deserve further attention because of their important public health implications.

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# Behavioral and Movement Disorders due to Long-Lasting Myoclonic Status Epilepticus Misdiagnosed as ADHD in a Patient With Juvenile Myoclonic Epilepsy: Electroclinical Findings and Related Hemodynamic Changes

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## Abstract

Epilepsy and attention-deficit/hyperactivity disorder (ADHD) likely share common underlying neural mechanisms, as often suggested by both the evidence of electroencephalography (EEG) abnormalities in ADHD patients without epilepsy and the coexistence of these 2 conditions. The differential diagnosis between epilepsy and ADHD may consequently be challenging. In this report, we describe a patient presenting with a clinical association of “tics” and behavioral disorders that appeared 6 months before our first observation and had previously been interpreted as ADHD. A video-EEG evaluation documented an electroclinical pattern of myoclonic status epilepticus. On the basis of the revised clinical data, the EEG findings, the good response to valproate, the long-lasting myoclonic status epilepticus, and the enduring epileptic abnormalities likely causing behavioral disturbances, the patient’s symptoms were interpreted as being the expression of untreated juvenile myoclonic epilepsy. The EEG–functional magnetic resonance imaging study revealed, during clinical generalized spike-and-wave and polyspike-and-wave discharges, positive blood oxygen level–dependent (BOLD) signal changes bilaterally in the thalamus, the prefrontal cortex (Brodmann area 6, supplementary motor area) and the cerebellum, and negative BOLD signal changes in the regions of the default mode network. Such findings, which are typical of BOLD changes observed in idiopathic generalized epilepsy, may also shed light on the anatomofunctional network underlying ADHD.

## Keywords

juvenile myoclonic epilepsy, attention-deficit/hyperactivity disorder, long-lasting myoclonic status epilepticus

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## Introduction

Epilepsy and ADHD are common neurological disorders affecting, respectively, 0.5% to 1% and 5% to 7% of the general population.<sup>1</sup> These 2 conditions likely share common underlying neural mechanisms, as has often been suggested by both the evidence of EEG abnormalities in ADHD patients without epilepsy and the existence of these two conditions in comorbidity.<sup>2</sup> Children with both epilepsy and ADHD may have an earlier seizure onset and higher frequency of seizures than children with epilepsy alone. Status epilepticus (SE) is more common and epilepsy is more often drug resistant in such children.<sup>3,4</sup> The differential diagnosis between epilepsy and ADHD may consequently be challenging: On one hand, behavioral changes such as inattention and hyperactivity are commonly reported in epileptic children; on the other hand, involuntary movements are, although rarely, associated with ADHD.<sup>5,6</sup> However, the relationship

between epilepsy and ADHD is complex and not well understood. The introduction of functional magnetic resonance imaging (fMRI) has allowed the investigation of cortical and subcortical brain regions involved in the pathophysiology of

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Full-color figures are available online at <http://eeg.sagepub.com>

**Table 1.** Neuropsychological Evaluation Before Neurological Assessment.

Type of Scale	Result
Colored progressive matrices (CPM) test	IQ: normal
Test of visual-motor integration (VMI)	Praxic-constructive ability: within normal limits
Test for the evaluation of dyslexia and developmental dysorthography (DDE-2)	Difficulty in reading speed; normal writing
Reading tests MT-2	Request for attention
Battery for dyscalculia (DBE-2 test)	Mental calculation: below normal
Vineland interview for adaptive behavior	Daily abilities and socialization: normal; communication: below normal
Test of everyday attention in children (TEA-Ch)	Sustained auditory attention: below normal
Test planning "Torre di Londra"	Organizational skills: below normal
Test of visual attention "Campanelle"	Sustained visual attention: below normal

both disorders. A resting-state fMRI study revealed, in both conditions, a significant deactivation of the regions of the so-called brain default mode network (DMN).<sup>7-9</sup> The DMN is a neural network active when the individual is not maintaining specific attention and the brain is at rest, and it can be variably attenuated in accordance with the difficulty of the performed task.<sup>10</sup> In this report, we describe a patient presenting with long-lasting myoclonic status epilepticus (MSE) documented by video-EEG and EEG-fMRI study. Before the EEG evaluation, cognitive/behavioral and movement disturbances related to the prolonged SE had been erroneously interpreted as ADHD.

## Case Study

### Methods

**Clinical Findings and Diagnosis Before Our Observation.** A 12-year-old boy was referred to our outpatient clinic because of a complex disorder characterized by cognitive and motor features. When he first came to our attention, he was being followed in a pediatric psychiatric clinic after the onset, 6 months earlier, of difficulties in reading and understanding written texts, mood alterations with anxiety and depression. The patient had already taken a battery of neuropsychological tests that included standard clinical measures of intelligence, praxic and constructive ability, academic skills, adaptation level and executive functions, and a comprehensive psychopathological evaluation, whose results had led to the diagnosis of predominantly inattentive ADHD. The results of each scale are synthetically shown in Tables 1 and 2. After some time, he had also developed involuntary rhythmic movements, which predominantly involved the upper limbs. In view of the patient's history of stammer, these motor phenomena had been interpreted as tics

**Table 2.** Psychopathological Evaluation Before Neurological Assessment.

Type of Scale	Result
Conner's Teacher Rating Scale (CTRS-R:L)	Cognitive problems/inattention, anxiety
Conner's Parent Rating Scale (CPRS-R:L)	Cognitive problems/inattention
Schedule for Affective Disorders and Schizophrenia (K-SADS)	Attention deficit/hyperactivity disorder predominantly inattentive, depressive disorder, generalized anxiety disorder
Children's Global Assessment Scale (C-GAS)	Academic performance difficulties, mood changes, fear, anxiety
Swanson, Nolan, and Pelham (SNAP-IV)	Inattention, 16; hyperactivity/impulsivity, 0; oppositional defiant disorder, 2
Multidimensional Anxiety Scale for Children (MASC)	General index of anxiety disorder within normal limits (physical symptoms, 17; harm avoidance, 16; social anxiety, 15; separation anxiety, 5)
Children's Depression Inventory (CDI)	Depressive symptoms (mood, 5; social relation, 8; negative self-view, 8)
Child Behavior Check List (CBCL 6-18)	Internalizing and externalizing problems

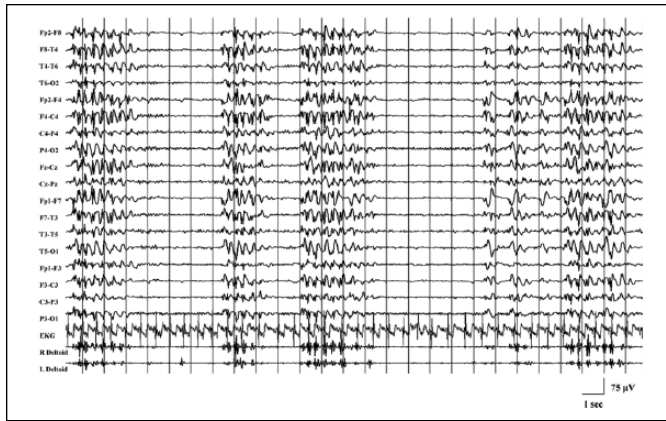
within the context of ADHD. The persistence and the intensity of movement disturbances suggested that further investigations were needed.

**Neurological Assessment at Our First Observation.** When the patient came to our attention for a reevaluation of his disorder, a video-EEG (Telefactor System, 21 channels, international 10-20 system) combined with a polygraphic study (deltoid muscles) and an MRI study were performed. On the basis of the electroclinical findings, we also decided to perform an ictal EEG/fMRI co-registration. This evaluation was performed according to the following methodological approach: Images were continuously acquired by using a 1.5-T magnet (Philips Gyroscan; 20 axial slices, 5 mm thickness, TR/TE = 3000/50 ms, image matrix 64 × 64, 2 series of 200 temporal dynamics, 10-minute scan time for each session); the EEG signal was acquired through a Micromed digital recording system (MR-compatible cap and head-box, optic cable, custom-developed software for off-line artifact removal); fMRI data were preprocessed (realigned and smoothed with Gaussian kernel 8 mm) and analyzed using SPM8 software (<http://www.fil.ion.ucl.ac.uk/spm>, Wellcome Department of Cognitive Neurology, London, UK).

## Results

Video-EEG monitoring, including polygraphy, performed in our laboratory documented an MSE with axial myoclonus, myoclonic





**Figure 1.** Myoclonic status epilepticus documented by video-EEG, showing the presence of sustained epileptic activity consisting of bilateral GSWDs and GPSWDs. The polygraphic study revealed subcontinuous myoclonic jerks involving the axial muscles, upper limbs, and eyelids. In this sample, the reduced polygraphic tracing shows myoclonus bilaterally involving deltoid muscles, closely related to epileptic abnormalities.

jerks involving the upper limbs and eyelid myoclonia associated with repetitive, continuous generalized spike-and-wave discharges (GSWDs) and generalized polyspike-and-wave discharges (GPSWDs) (Figure 1). The structural MRI was normal. After a careful revision of all the electroclinical and neuroimaging findings, a diagnosis of juvenile myoclonic epilepsy (JME) was made.

The fMRI data revealed significant BOLD signal changes related to EEG abnormalities. More specifically, we identified the main activation clusters bilaterally in the thalamus, prefrontal cortex (Brodmann area 6 [BA6], supplementary motor area [SMA]) and cerebellum, and the main deactivation clusters in the DMN regions (Figure 2).

Administration of intravenous valproate during the video-EEG monitoring led to the prompt disappearance of the myoclonic phenomena and EEG abnormalities. Antiepileptic drug treatment subsequently also led to an improvement in the child's psychocognitive disorders. Following the disappearance of the myoclonic phenomena and EEG abnormalities, the child's family and teachers reported a marked improvement in his academic performance and attentional capacity. The patient underwent a comprehensive neuropsychological and psychopathological assessment that showed a multidimensional improvement in the functions examined, although a slight mood disorder persisted.

## Discussion

Epilepsy and ADHD are 2 common neurological disorders that may have important negative consequences on a child's behavioral, learning, and social development. Data in the literature reveals that at least 20% of epileptic children display ADHD-like clinical features.<sup>1</sup> Some hypotheses have been made to explain this association. First, brain damage may be responsible for both epilepsy and alterations in cognition and behavior in children. Second, persistent epileptic activity, such as status

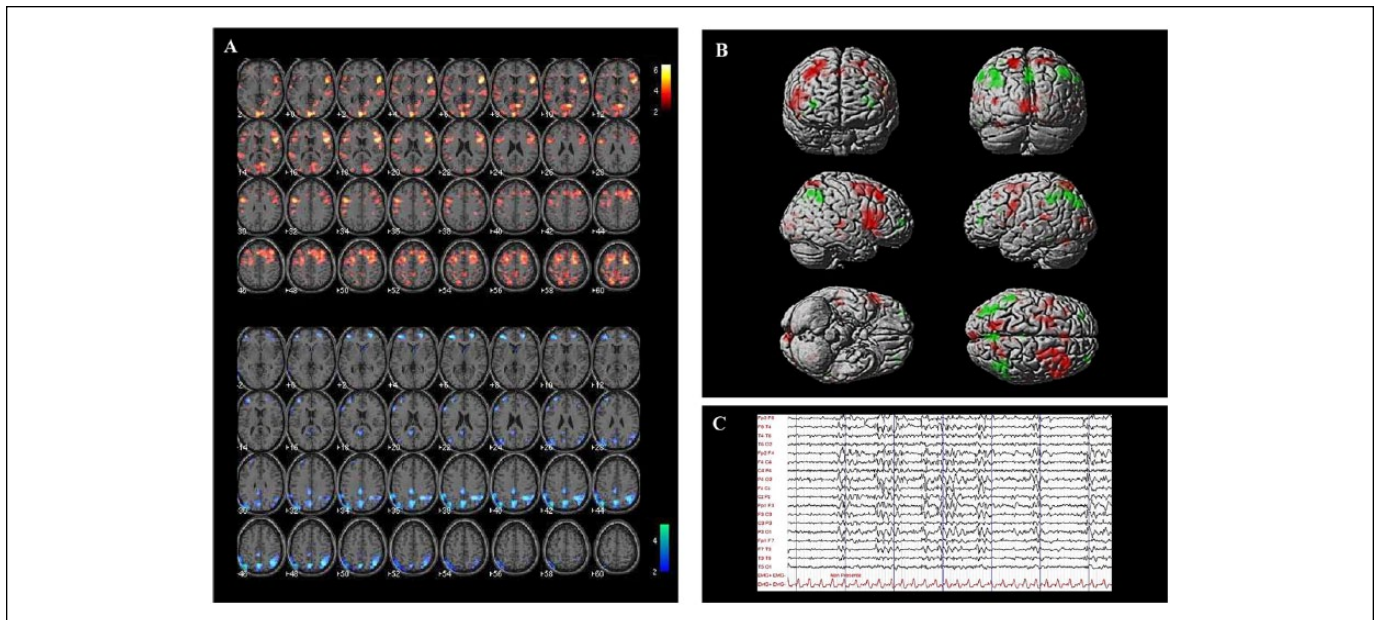
epilepticus, nonconvulsive status epilepticus during slow-wave sleep and frequent interictal epileptiform discharges, may significantly contribute to neuropsychological disorders by functionally interfering with normal brain development.<sup>11</sup>

Moreover, ADHD coexists in 30% to 40% of epileptic children: Behavioral/cognitive manifestations may often precede the onset of epilepsy.<sup>12</sup> In some specific epileptic syndromes, such as frontal lobe epilepsy, childhood absence epilepsy, and Rolandic epilepsy, the association with ADHD is significantly more frequent. Epilepsy in patients with comorbid ADHD appears to be more severe than in those with epilepsy alone: SE is more common, seizures are often drug resistant and progression of epilepsy is faster.<sup>3</sup> Moreover, approximately 5.4% of children with ADHD alone are reported to have epileptiform abnormalities in the EEG.<sup>2</sup>

The complex relationship between ADHD and epilepsy points to the involvement of common neural networks.<sup>7-9</sup> To gain a better knowledge of the underlying neural mechanisms, both conditions are currently being studied by means of new neuroimaging approaches, including functional techniques that investigate networks involved in a range of neurological disorders.<sup>13</sup>

In our case, the EEG-fMRI recording revealed, during GSWDs and GPSWDs, the most significant activation in the thalamus bilaterally, while the most significant deactivation was observed in the areas involved in the brain DMN. This pattern of activation-deactivation is similar to that commonly observed in absence seizures within the context of idiopathic generalized epilepsy.<sup>14</sup> Indeed, a BOLD increase has been detected bilaterally in the thalamus, cerebellum, and anterior cingulate gyrus during 3-Hz GSWDs. Contemporarily, a BOLD decrease has been documented bilaterally in the lateral parietal lobe, middle and posterior cingulate gyrus, and precuneus, which represent the so-called DMN.<sup>15</sup> Deactivation of the DMN occurs during GSWDs and GPSWDs and may be responsible for the reduced consciousness during absence seizures.<sup>14</sup>

However, if compared with the pattern of absence seizures, the activation clusters in our patient also include the prefrontal (BA6, SMA) and perisylvian cortex, probably as a result of the spreading of the epileptic discharges. This finding is in accordance with neurophysiological, neuropsychological and imaging studies performed in patients with JME, which reveal an involvement of frontal motor circuits. Indeed, in patients with JME, co-activation of the primary motor cortex and SMA during cognitive tasks, which has been demonstrated by fMRI studies, is probably related to an increased functional connectivity between the motor system and frontoparietal cognitive networks.<sup>8</sup> The functional hemodynamic changes observed in our case involve brain regions that are hypothesized to be involved in the complex neural network of ADHD. Patients with ADHD are reported to have both structural and functional abnormalities associated with the DMN. Structural MRI studies have documented volumetric reductions in the frontal lobes, posterior and anterior cingulate gyri, precentral gyrus, caudate nuclei, corpus callosum, and cerebellum.<sup>7</sup> In ADHD patients, fMRI studies have demonstrated atypical functional activations in the frontal, temporal, and parietal lobes and in the cerebellum.<sup>9</sup>



**Figure 2.** Epileptic activity–related hemodynamic changes observed in the EEG/fMRI study. The fMRI analysis shows a significant cluster of activation (red scale) involving the thalamus, the prefrontal (BA6, SMA) and perisylvian cortex, and a cluster of deactivation (blue or green scale) involving the DMN. Statistical parametric maps thresholded at  $P < .05$  (corrected for multiple comparisons FWE [family-wise error]) are superimposed on a structural image (A) and on a template brain surface (B). EEG recording performed within the scanner after suppression of the gradient artefacts (C).

## Conclusion

This original case is highly interesting since it offers the possibility to explore the complex relationship between epilepsy and ADHD, 2 very common disorders that may share neural mechanisms. However, further studies on similar cases are required to support the hypothesis that common cerebral networks may underlie 2 such distinct pathologies. Our case may, however, be useful in daily clinical practice insofar as it points to the need to carefully evaluate, by clinical and EEG examinations, young patients affected by ADHD or other neuropsychological disorders, particularly those presenting with atypical features, since persistent epileptic activity may “mimic” these conditions. Finally, this is, to our knowledge, the first reported case of an EEG–fMRI study performed during MSE, which is itself a very rare condition in patients with JME.

## Author Contributions

MF contributed to conception and design; contributed to acquisition, analysis, and interpretation; drafted manuscript; gave final approval; agrees to be accountable for all aspects of work ensuring integrity and accuracy. MC contributed to design; contributed to analysis; critically revised manuscript; gave final approval; agrees to be accountable for all aspects of work ensuring integrity and accuracy. AM contributed to acquisition and interpretation; drafted manuscript; critically revised manuscript; gave final approval; agrees to be accountable for all aspects of work ensuring integrity and accuracy. MA contributed to design; critically revised manuscript; gave final approval; agrees to be accountable for all aspects of work ensuring integrity and accuracy. LL contributed to analysis and

interpretation; critically revised manuscript; gave final approval; agrees to be accountable for all aspects of work ensuring integrity and accuracy. SC contributed to acquisition, analysis, and interpretation; critically revised manuscript; gave final approval; agrees to be accountable for all aspects of work ensuring integrity and accuracy. JF contributed to interpretation; critically revised manuscript; gave final approval; agrees to be accountable for all aspects of work ensuring integrity and accuracy. EDC contributed to analysis; critically revised manuscript; gave final approval; agrees to be accountable for all aspects of work ensuring integrity and accuracy. CC contributed to interpretation; critically revised manuscript; gave final approval; agrees to be accountable for all aspects of work ensuring integrity and accuracy. AEV contributed to conception and design; critically revised manuscript; gave final approval; agrees to be accountable for all aspects of work ensuring integrity and accuracy. ATG contributed to conception; critically revised manuscript; gave final approval; agrees to be accountable for all aspects of work ensuring integrity and accuracy. CDB agrees to be accountable for all aspects of work ensuring integrity and accuracy; contributed to interpretation; drafted manuscript; critically revised manuscript; gave final approval; agrees to be accountable for all aspects of work ensuring integrity and accuracy.

## Declaration of Conflicting Interests

The author(s) declared no conflicts of interest with respect to the research, authorship, and/or publication of this article.

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di Karen Rubin

## Qui e Ora

## Adhd, una patologia non certo una «bufala»

Periodicamente, sui siti di disinformazione medica e scientifica, rispunta una falsa notizia su una psicopatologia dell'età evolutiva: l'Adhd, deficit di attenzione e iperattività, sarebbe una malattia fittizia, in altre parole inventata e del tutto inesistente, ma per la quale un esercito di bambini sani in tutto il mondo sarebbe sottoposto a cure inutili e dannose per la salute. Non è difficile immaginare quanta confusione possa generare, in un genitore che ha un figlio che ne è affetto, la lettura di questa fandonia che imperversa sul web. Anni fa ci cascò il Daily Mail, uno dei maggiori quotidiani britannici, ma ci cascano ancora oggi medici e giornalisti poco informati che finiscono per accreditare la bufala postandola sui social network. La cosa incredibile è che la notizia è rilanciata ciclicamente da un'organizzazione che si chiama Ccdu, Comitato dei cittadini per i diritti umani. È assurdo siano loro a ergersi a difensori della salute mentale quando Scientology, cui sono ideologicamente collegati, si fonda su una credenza fantascientifica del suo fondatore L. Ron Hubbard: per esprimere tutte le nostre potenzialità dobbiamo liberare le nostre anime da immagini traumatiche che si sono impossessate di noi a causa di un'antica invasione extraterrestre. Per localizzare queste immagini negative e per eliminarle servono tecniche molto costose che Scientology conosce ed elargisce a pagamento solo ai suoi adepti. Anche siti antibufala come Butac.it e Bufale e Dintorni di Sandro Martone hanno smentito la notizia. Il Ccdu scrive che il professor Leon Eisenberg, che

indicano sbagliando come lo scopritore dell'Adhd, sul punto di morire confessò di averla letteralmente inventata. Invitò i medici a indagare le cause ambientali che possono determinarla, come disagi familiari e sociali, invece di ritenere che possa essere causata da un deficit neurobiologico. Questa intervista, rilasciata da Eisenberg, fu pubblicata sulla rivista tedesca *Der Spiegel*, ed è utilizzata strumentalmente dai movimenti antipsichiatrici, tra cui il Ccdu. Su Bufale e Dintorni, il debunker Marilena Pozzi, traduce correttamente dal tedesco all'italiano l'intervista del professore spiegando cosa intendesse realmente. Egli non affermò che la malattia fosse inventata ma disse che alcuni medici la diagnosticano con troppa facilità e che con la stessa facilità prescrivono la terapia medica anche quando il bambino non ne ha bisogno. Un problema, quello delle diagnosi affrettate ed errate, che non riguarda solo l'Adhd, e che non significa che il disturbo non sia reale. È reale, dimostrato da numerose ricerche e costituisce una patologia che se non è affrontata adeguatamente può portare con sé un deficit cognitivo, scolastico e di comportamento. Un neuropsichiatra infantile e ogni genitore che guardi davvero alla salute mentale del figlio può distinguere tra un'esuberanza motoria ed una incapacità di concentrarsi che rientra nella normalità e non va assolutamente curata da quella che diventa un serio ostacolo per la crescita del bambino, che non gioca, non impara e non ha amici con cui condividere affetto, tempo libero e sport. Un ostacolo alla sua felicità, cui bisogna porre rimedio.





## Questionario per la valutazione della Newsletter ADHD



Gent.mi lettori,

questo è un invito alla compilazione del questionario on-line sulla Newsletter ADHD.

Tale operazione Vi impegnerà per 2 minuti al massimo accedendo al seguente link:

<http://www.adhd.marionegri.it/index.php/newsletter/valutazione-newsletter>

Si confida nella Vs preziosa collaborazione.



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Iniziativa nell'ambito del Progetto di Neuropsichiatria dell'Infanzia e dell'Adolescenza  
(Delibera n. 406 - 2014 del 04/06/2014 Progetti NPI)  
Il Progetto è realizzato con il contributo, parziale, della Regione Lombardia  
(in attuazione della D.G. sanità n. 3798 del 08/05/2014 e n. 778 del 05/02/2015)  
Capofila Progetto: UONPIA Azienda Ospedaliera "Spedali Civili di Brescia" *"Percorsi  
diagnostico-terapeutici per l'ADHD"*.