NEWSLETTER

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ISTITUTO DI RICERCHE FARMACOLOGICHE MARIO NEGRI IRCCS

BIBLIOGRAFIA ADHD MAGGIO 2018

Acta Paediatr Int J Paediatr. 2018.

LOWER APGAR SCORES AND CAESAREAN SECTIONS ARE RELATED TO ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.

Sucksdorff M, Lehtonen L, Chudal R, et al.

Aim: We examined the associations between prenatal, birth-related and newborn risk factors and attention-deficit/hyperactivity disorder (ADHD).

Methods: In this population-based study, 10 409 subjects diagnosed with ADHD by 31 December 2011 and 39 124 controls, born between 1 January 1991 and 31 December 2005, were identified from Finnish nationwide registers. Perinatal data were obtained from the Birth Register. Conditional logistic regression was used to examine the associations after controlling for confounders.

Results: Lower Apgar scores were associated with a higher risk of ADHD, with odds ratios of 1.12 (95% confidence intervals 1.06-1.19) for one-minute Apgar scores of 7-8, 1.17 (95% CI 1.02-1.35) for scores of 5-6 and 1.41 (95% CI 1.18-1.68) for scores of 0-4, compared to Apgar scores of 9-10. Elective Caesarean sections were associated with an increased risk of ADHD with an adjusted odds ratio of 1.15 (95% CI 1.05-1.26). Other identified risk factors were breech presentation, induced labour and admission to a neonatal intensive care unit. Low umbilical artery pH did not increase the risk of ADHD.

Conclusion: Elective Caesareans and perinatal adversities leading to lower Apgar scores increased the risk of ADHD. Future research to identify the mechanisms behind these findings is warranted

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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.

An Pediatr. 2018;88:191-95.

DO CHILDREN WITH ATTENTION DEFICIT AND HYPERACTIVITY DISORDER (ADHD) HAVE A DIFERENT GAIT PATTERN? RELATIONSHIP BETWEEN IDIOPATHIC TOE-WALKING AND ADHD.

Soto I, V, Moreno VsB, Losada del PR, et al.

Introduction: Idiopathic toe-walking (ITW) is described as a gait pattern with no contact between the heels and the ground in children older than 3 years. The diagnosis is clinical, making it necessary to rule out other neurological and orthopaedic conditions. A relationship between ITW and vestibular dysfunction and/or proprioceptive sensibility has been proposed. Children with neurodevelopmental disorders (autism, language and cognitive disorders) often have ITW.

Objectives: To determine the frequency of ITW in children with attention deficit disorder and hyperactivity (ADHD).

Patients and method: A study was conducted on children diagnosed with ADHD, with normal neurological examination, with no alterations in MRI scan, cognitive disorder or autism. A complete clinical anamnesis was performed and Achilles shortening was measured with a goniometer.

Results: The study included 312 children with a mean age of 11 years (73.7% boys). The ADHD combined subtype was the most frequent (53.8%), followed by the inattentive (44.9%), and hyperactive (1.3%). ITW was observed in 20.8% of patients, particularly in the combined subtype (P=.054). Only 32 of them (49.2%) had Achilles shortening. ITW was associated with sociability disorders (P=.01), absence of pain in legs (P=.022), and family history of ITW (P=.004). Only 11% had previously visited a doctor for this reason.

Conclusions: As in other neurodevelopmental disorders, children with ADHD have frequently more ITW and Achilles shortening than controls, especially if they presented with a social communication disorder or a family history of ITW. An early diagnosis is essential to establish effective treatments

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An Pediatr. 2018;88:183-90.

THE EPIDEMIOLOGY OF PHARMACOLOGICALLY TREATED ATTENTION DEFICIT HYPERACTIVITY DISORDER (ADHD) IN THE REGION OF MURCIA, SPAIN: DIFFERENCES BY GENDER, AGE AND LOCATION OF RESIDENCE.

Sánchez Martínez DP, Guillén Pérez JJ.

Introduction: Attention deficit hyperactivity disorder (ADHD) is the most frequent disorder in childhood and adolescence, and is seen as a public health problem. The recommended treatment includes pharmacological and psychosocial treatment. The aim of this work was to study the changes in the prescribing of the medicines used in ADHD treatment in the Region of Murcia, as well as their socio-demographic variability.

Method: A retrospective observational study was conducted using the dispensing of medicines for ADHD treatment by means of prescription in the Region of Murcia from 2010 to 2014. The consumption rates were determined as defined daily doses (DDD) per thousand inhabitants/day (DHD), stratified by gender and age. The reasons for prevalence of treatment by gender were also determined by comparing male and female consumption rates.

Results: The consumption of medicines for ADHD treatment had almost doubled in the period studied, from 5.58 DHD and 3.39 DHD in 2010 to 9.34 DHD and 6.71 DHD in 2014, for the age range of 10-14 and 15-19, respectively. Boys from 10-14 showed the highest consumption rates, showing a high geographical variability with less consumption in rural areas.

Conclusion: The results showed a large increase in the use of medicines for ADHD treatment in the Region of Murcia, although the consumption rates are still lower than in other Autonomous Communities or neighbouring countries. A wide geographical variability was found, with a higher consumption in adolescents from urban areas

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Appetite. 2018;127:274-79.

ASSOCIATIONS BETWEEN ATTENTION-DEFICIT/HYPERACTIVITY DISORDER SYMPTOMS AND DIETARY HABITS IN ELEMENTARY SCHOOL CHILDREN.

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

Objective: The aim of the present study was to investigate the associations between dietary habits and attention deficit/hyperactivity disorder (ADHD) symptoms in elementary school children.

Methods: The parents of 16,831 participating children assessed the ADHD symptoms of their children by responding to the Korean version of the ADHD rating scale (K-ARS). Parents also responded to the food habit questionnaire, which consists of 8 items regarding the eating pace, the frequency of overeating, and patterns of eating six types of food: fast food, soft drinks, instant noodles, fruit and vegetables, and milk.

Results: K-ARS scores were positively associated with higher consumption of foods categorized as unhealthy, including fast food, soft drinks, and instant noodles, and negatively associated with higher consumption of fruit and vegetables categorized as healthy foods. K-ARS scores were also higher in the groups who overate more frequently and ate faster or slower compared to other family members.

Conclusion: Our findings may provide useful clinical information for dietary interventions in children with ADHD

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Appl Neuropsychol Child. 2018 Apr;7:150-56.

EVIDENCE-BASED ASSESSMENT OF ADHD DIAGNOSIS IN CHILDREN AND ADOLESCENTS.

Zhou X, Reynolds CR, Zhu J, et al.

This study illustrates the accuracy and efficiency of using an evidence-based assessment (EBA) strategy for diagnosis of attention-deficit/hyperactivity disorder (ADHD) by integrating the scale scores obtained on BASC-3 teacher and parent rating scales. The examined process used empirical diagnostic likelihood ratios (DLRs) derived from a sample of children with ADHD (N = 339) matched on demographic characteristics from the normative sample. The results show that behavioral scales of executive functioning and functional communication provided incremental utility in ADHD diagnosis. With a revised probability of .80 or higher as the diagnostic criterion, teachers, and parents positively diagnosed 70% and 94% of the ADHD cases respectively. The EBA approach was efficient, with four scales on average used to reach the proposed posterior probability for final diagnosis. Finally, teachers and parents demonstrated a high agreement with respect to the diagnosis results and scales used for the diagnosis

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Autism. 2018;22:502-12.

JOINT ATTENTION DIFFICULTIES IN AUTISTIC ADULTS: AN INTERACTIVE EYE-TRACKING STUDY.

Caruana N, Stieglitz HH, Brock J, et al.

Joint attention ΓÇô the ability to coordinate attention with a social partner ΓÇô is critical for social communication, learning and the regulation of interpersonal relationships. Infants and young children with autism demonstrate impairments in both initiating and responding to joint attention bids in naturalistic settings. However, little is known about joint attention abilities in adults with autism. Here, we tested 17 autistic adults and 17 age- and nonverbal intelligence quotientΓÇômatched controls using an interactive eye-tracking paradigm in which participants initiated and responded to joint attention bids with an on-screen avatar. Compared to control participants, autistic adults completed fewer trials successfully. They were also slower to respond to joint attention bids in the first block of testing but performed as well as controls in the second block. There were no group differences in responding to spatial cues on a non-social task with similar attention and oculomotor demands. These experimental results were mirrored in the subjective reports given by participants, with some commenting that they initially found it challenging to communicate using eye gaze, but were able to develop strategies that allowed them to achieve joint attention. Our study indicates that for many autistic individuals, subtle difficulties using eye-gaze information persist well into adulthood

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Behav Ther. 2018.

PREDICTORS AND TRAJECTORIES OF RESPONSE TO THE HOMEWORK, ORGANIZATION, AND PLANNING SKILLS (HOPS) INTERVENTION FOR ADOLESCENTS WITH ADHD.

Breaux RP, Langberg JM, Molitor SJ, et al.

The goal of the present study was to evaluate the relative importance of adolescent and parent skills acquired during participation in the Homework, Organization, and Planning Skills (HOPS) intervention in predicting intervention response. A sample of 111 middle school students with attention-deficit/hyperactivity disorder (66% male; Mage = 11.99, SD = 1.05) received the HOPS intervention, which includes 16 brief sessions with the adolescent and two parent meetings. Each session, school mental health providers completed checklists measuring studentsΓÇÖ acquisition of homework recording, materials organization, and time management skills. Parents provided information on whether they monitored and used contingencies to reinforce skills use at home. Outcome measures included parent and teacher ratings of homework problems and organizational/time management skills postintervention. Grade point average and assignment completion were also evaluated as objective outcomes. Regressions found accurate homework recording and time management to be unique predictors of parent-reported homework and organizational skills outcomes. Growth mixture models examining organizational skills trajectories throughout the intervention significantly predicted parent- and teacher-reported outcomes, GPA, and assignment completion; homework recording trajectories predicted parent-reported outcomes and GPA. Sixty-eight percent of participants displayed high acquisition of organization and homework recording skills. Parent-reported use of monitoring and contingencies to support adolescent skills implementation was not associated with outcomes. Results highlight the importance of examining individual differences in school-based intervention studies targeting organization, time management, and planning. Importantly, for a school-based adolescent-focused intervention, improvement in outcomes does not appear to be dependent upon parent skills implementation

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Behav Ther. 2018.

IMPROVED PARENT COGNITIONS RELATE TO IMMEDIATE AND FOLLOW-UP TREATMENT OUTCOMES FOR CHILDREN WITH ADHD-PREDOMINANTLY INATTENTIVE PRESENTATION.

Jiang Y, Haack LM, Delucchi K, et al.

We investigated treatment effects on parenting self-efficacy and parent cognitive errors, and whether these parent cognitions are related to short- and long-term outcomes in parenting behaviors in psychosocial treatment for youth with attention-deficit/hyperactivity disorder, predominantly inattentive presentation (ADHD-I). In a randomized controlled trial across two sites (University of California, San Francisco, and University of California, Berkeley), 199 children between the ages of 7 and 11 were randomized to the Child Life and Attention Skills (CLAS; n = 74) program, parent-focused treatment (PFT; n = 74), or treatment as usual (TAU; n = 51). Parents reported on self-efficacy, cognitive errors, positive parenting, and negative parenting prior to treatment, immediately after treatment, and in the next school year at follow-up. Compared to TAU, CLAS and PFT had higher posttreatment parenting self-efficacy, and CLAS alone had lower posttreatment parent cognitive errors. At follow-up, only CLAS had improved parent cognitive errors compared to TAU. No other between-group differences were found in parenting self-efficacy or cognitive errors. Improved parenting self-efficacy was associated with improved posttreatment negative parenting outcomes for PFT and CLAS, and improved parent cognitive errors were also related to improvements in positive and negative posttreatment parenting outcomes for CLAS. Posttreatment parenting self-efficacy mediated follow-up negative parenting outcomes for CLAS and posttreatment parent cognitive errors mediated improved follow-up positive and negative parenting outcomes for CLAS. PFT and CLAS led to enhanced parenting self-efficacy, and CLAS appears especially robust in improving parent cognitive errors both in the short and long term. Pathways provide support for the possibility of parent cognitions as mediators of treatment effects on parenting; clinical focus on such cognitions may be useful

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Behav Brain Funct. 2018;14.

ASSESSING ADHD SYMPTOMS IN CHILDREN AND ADULTS: EVALUATING THE ROLE OF OBJECTIVE MEASURES.

Emser TS, Johnston BA, Steele JD, et al.

Background: Diagnostic guidelines recommend using a variety of methods to assess and diagnose ADHD. Applying subjective measures always incorporates risks such as informant biases or large differences between ratings obtained from diverse sources. Furthermore, it has been demonstrated that ratings and tests seem to assess somewhat different constructs. The use of objective measures might thus yield valuable information for diagnosing ADHD. This study aims at evaluating the role of objective measures when trying to distinguish between individuals with ADHD and controls. Our sample consisted of children (n = 60) and adults (n = 76) diagnosed with ADHD and matched controls who completed self- and observer ratings as well as objective tasks. Diagnosis was primarily based on clinical interviews. A popular pattern recognition approach, support vector machines, was used to predict the diagnosis.

Results: We observed relatively high accuracy of 79% (adults) and 78% (children) applying solely objective measures. Predicting an ADHD diagnosis using both subjective and objective measures exceeded the accuracy of objective measures for both adults (89.5%) and children (86.7%), with the subjective variables proving to be the most relevant.

Conclusions: We argue that objective measures are more robust against rater bias and errors inherent in subjective measures and may be more replicable. Considering the high accuracy of objective measures only, we found in our study, we think that they should be incorporated in diagnostic procedures for assessing ADHD

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Biol Psychiatry. 2018;83:S364.

EARLY COMMUNITY-BASED SERVICES AND TRAJECTORIES OF BEHAVIORAL PROBLEMS AMONG CHILDREN WITH VARYING LEVELS OF INATTENTION/HYPERACTIVITY-IMPULSIVITY.

Rajendran K, O'Neill S, Richards S, et al.

Background: Randomized controlled trials provide evidence for medications and behavior modification to treat Attention-Deficit/Hyperactivity Disorder (ADHD). However, few naturalistic studies have assessed the impact of early medication and school-based services on longitudinal changes in behavior.

Methods: Preschoolers (N=216) were recruited at 3-4 years old (T0): 140 had-6 inattentive and/or hyperactive symptoms; 76 had < 3 symptoms (ADHD status). Children's service use (ADHD Medication, behavioral counseling, Occupational, Physical and Speech therapy, and Special Educational Services; N=201) was assessed at 4-5 years (T1). Teachers rated behavior annually (T1-T7) using the BASC-2. Latent Class Analysis (LCA) was used to classify children based on their ADHD status and T1 services received. These classes were used as predictors in a longitudinal growth model of behavioral trajectories.

Results: Three groups emerged: Group 1 [N=116; Mean(SD) T1 ADHD symptoms=10.71 (9.99)] included children who were least likely to receive any treatment; Group 2 (N=60; Mean(SD) T1 ADHD symptoms=18.71 (11.17)] were most likely to receive school-based services; Group 3 (N=25; Mean(SD) T1 ADHD symptoms=30.25(8.97)] were most likely to receive medication and other services. Latent variable growth modeling showed that teacher-rated Inattention, Hyperactivity and Aggression were highest at T1 in Group 3 which also had a significantly greater decline in all behaviors than Group 1 and showed greater decrease in Aggression than Group 2. Rate of change was not different between Groups 1 and 2.

Conclusions: Behavioral improvements are greater among children who receive comprehensive, early services relative to those who do not

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Biol Psychiatry. 2018;83:S121.

AGE-NORMATIVE PATHWAYS OF STRIATAL CONNECTIVITY RELATE TO ADHD SYMPTOMS IN THE GENERAL POPULATION.

Barber A, Sarpal D, John M, et al.

Background: Altered striatal development contributes to core deficits in motor and inhibitory control, impulsivity, and inattention associated with ADHD. Previous studies examining the development of striatal connectivity do not adequately sample various developmental stages to assess both linear and nonlinear age effects.

Methods: Resting state fMRI and T1-weighted scans were collected for the Pediatric, Imaging, Neurocognition and Genetics (PING) study and the Philadelphia Neuroimaging Cohort (PNC). 1215 neurotypical participants (ages 3-22 years) had usable resting-state data. Six 4-mm seeds were placed in striatal subdivisions in each hemisphere. Models assessed linear and nonlinear age effects and accounted for Frame-wise Displacement (FD), FD-squared, and site. A growth-charting approach was applied to the Developing Striatal Connections (DSCs). Age-deviation scores were computed from the 50th percentile (i.e. age-normative) fit line and Principal Component Analysis (PCA) was performed to identify age-normative patterns of striatal connectivity.

Results: PCA on the age deviation scores from the set of DSCs revealed four striatal pathways of normative development. Using permutation testing (10,000 permutations), associations were found between PCA component 2 and ADHD measures (ADHD liability: $b = 0.014$, $p = 0.0032$; inattention: $b = 0.020$, $p = 0.0016$).

Conclusions: Age-normed striatal connectivity related to ADHD symptoms and reflected delayed development for several intra-striatal and striatal-cerebellar connections, but accelerated development for a few intra-caudate and striatal-posterior OFC connections. Developmental overreactivity in this limbic circuitry could underlie reward reactivity, impulsivity, and poor emotion regulation associated with ADHD

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Biol Psychiatry. 2018;83:S151.

DOES WHITE MATTER MICROSTRUCTURAL INTEGRITY DIFFER IN THE COMBINED AND INATTENTIVE SUBTYPES OF ADHD? A DIFFUSION TENSOR IMAGING STUDY.

Saad J, Griffiths K, Kohn M, et al.

Background: Converging evidence indicates that dysfunctional brain network connections are concordant with aberrant neuroanatomical and functional features; these findings extend support for differential neural mechanisms underlying the ADHD subtypes. However, diffusion tensor imaging (DTI) studies investigating microstructural white matter (WM) properties between the ADHD subtypes are limited and have shown equivocal results.

Methods: We used DTI data from 35 ADHD participants defined using DSM-IV criteria as combined (n=19) or as predominantly inattentive type (n=16), aged 8-17 years, and 28 matched neurotypical controls. We performed tract-based spatial statistical (TBSS) analyses on DTI derived measures of fractional anisotropy (FA), mean (MD), radial (RD), and axial (AD) diffusivity to assess differences in WM microstructural integrity between the two ADHD subtypes and controls.

Results: DTI measures (FA, MD, RD, and AD) were not found to differ significantly between the ADHD subtypes, or for each subtype relative to controls. This null finding was observed in the context that the same ADHD subtypes were distinguished by grey matter organization, as quantified by structural covariance.

Conclusions: Adding to the paucity of DTI studies examining ADHD subtypes, this study did not observe WM differences that may distinguish the ADHD subtypes. Given our observation of grey matter disorganization in the absence of loss of white matter integrity, anatomical network patterns may better account for the clinical symptoms that characterize the ADHD subtypes

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Biol Psychiatry. 2018;83:S31-S32.

INTRINSIC BRAIN ARCHITECTURE PREDICTS FUTURE ATTENTIONAL AND MOOD PROBLEMS IN A NORMATIVE PEDIATRIC SAMPLE.

Whitfield-Gabrieli S, Bailey S, Cutting L, et al.

Background: Previously we and others have discovered ways in which neuroimaging could be used to identify brain network pathologies in children who are at familial risk for psychiatric disorders but who are not currently diagnosed with any disorder. Here, we expand on the previous findings by investigating longitudinally a normative sample of children.

Methods: We tested whether resting state fMRI, can predict individual children's developmental trajectories towards attentional problems characteristic of Attention Deficit Hyperactivity Disorder (ADHD), or internalizing problems characteristic of major depression (MDD). We analyzed neuroimaging and behavioral data from a longitudinal study of children assessed at age 7 (N=94), and again at age 11 (N=54). We tested whether specific connectivity patterns would predict scores on the Child Behavior Checklist (CBCL), a parental report assessment used to screen for behavioral problems and to predict psychiatric illnesses.

Results: Greater connectivity at age 7 between medial prefrontal cortex (MPFC), a core node in the default mode network (DMN), and dorsolateral prefrontal cortex (DLPFC) predicted the development of attentional problems characteristic of ADHD by age 11. Weaker connectivity between a region implicated in mood, the subgenual anterior cingulate cortex (sgACC), and DLPFC at age 7 predicted the development of internalizing behaviors by age 11.

Conclusions: These findings further our understanding of the neurobiological vulnerabilities that foster the deterioration of mental health, but also could inform early identification and preventative treatment for children who, regardless of a documented family history of mental disorders, have a neurobiological vulnerability for ADHD or MDD

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Biol Psychiatry. 2018;83:S118-S119.

BRAIN SIGNATURES OF EMOTIONAL LABILITY AND ADHD TRAITS IN YOUNG CHILDREN.

Rohr C, Webber A, Dimond D, et al.

Background: 40-50% of children with ADHD present with significant levels of emotional lability, which is associated with poorer outcomes. Characterizing emotional lability in relation to the diagnostic dimensions of inattention and hyperactivity is therefore critical for the development of effective treatments. As a starting point, we here investigated the brain basis of these relationships using functional connectivity (FC) analyses in 58 typically developing children aged 4- 7 years.

Methods: Children watched a TV show while fMRI data was acquired, and regional time courses were correlated to estimate FC. Emotional lability was assessed with the Emotion Regulation Checklist; inattention and hyperactivity were assessed with the SNAP-IV Parent Questionnaire. To identify shared and distinct neural pathways, we used data-driven connectome-based predictive modelling to develop models of inattention, hyperactivity and emotional lability from the connectivity data.

Results: Emotional lability scores correlated with both inattention ($r=.68$, $p<0.001$) and hyperactivity scores ($r=.66$, $p<0.001$); inattention and hyperactivity were also correlated ($r=.8$, $p<0.001$). FC associated with all three scores revolved around pathways between midbrain-thalamus and the default mode network. In addition, emotional lability and inattention exclusively shared pathways within the dorsal attention network and its connections to hippocampus and dorsolateral prefrontal cortex; emotional lability and hyperactivity exclusively shared thalamostriatal connections, as well as connections between hippocampus and sensory areas.

Conclusions: Our findings suggest that multiple brain pathways underlie the link between emotional lability and ADHD traits in early childhood. Further, they demonstrate the utility of dimensional (continuous) scores and multivariate predictive modelling to interrogate brain-behavior relationships in young children

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Biol Psychiatry. 2018;83:S309-S310.

DAYDREAMING AND DEPRESSION: THE RESPONSE TO STIMULANTS.

Nasr S, Coyle J, Wendt B.

Background: Daydreaming is common in both childhood and adulthood. In children with ADHD, inattentive type particularly, it contributes to their distractibility. Stimulants are the standard treatment for ADHD, but there is no data on the preferential benefit of stimulants for depressed adults who also frequently daydreamed as children.

Methods: A retrospective chart review was performed on patients in a private outpatient psychiatric clinic. Data collected included demographics, medication history, answers to how frequently they daydreamed in school, PHQ-9 scores from every visit, and their current diagnoses.

Results: Over a three-year period, 217 patients completed the initial questionnaire. Of these, 80 reported they had daydreamed frequently or continuously as a child. Clinical depression was diagnosed in 67% of the continuous daydreamers, 44% of the frequent daydreamers and 23% of those who never daydreamed. ADD was diagnosed in 38% of the continuous daydreamers, 32% of frequent daydreamers, and 16% of occasional or never daydreamers. When the continuous daydreamers were treated with stimulants, their depression remitted more effectively as measured by most recent PHQ-9 score (5.8 vs. 12.9, p<.08, PHQ at intake of 16.4).

Conclusions: Childhood daydreamers in this patient population were more likely to be diagnosed with depression in adulthood and more likely to respond to stimulants. There is increasing awareness that overlapping symptoms of what appear to be unrelated diagnoses may have the same biological origins and may thus respond to the same treatments. This data raises the possibility that there is shared neurocircuitry between daydreaming in childhood and later onset of depression

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Biol Psychiatry. 2018;83:S263-S264.

INCREASED AMYGDALAR ACTIVATION TO ANGRY FACES IS LINKED TO REDUCED PREFRONTAL CORTICAL THICKNESS AND HYPERACTIVE/INATTENTIVE SYMPTOMATOLOGY IN ADOLESCENTS.

Albaugh M, Orr C, Spechler P, et al.

Background: Prior studies have reported increased amygdalar activation in response to emotional stimuli among individuals with attention-deficit/hyperactivity disorder (ADHD). Herein, we investigate the extent to which amygdalar activation to angry faces is associated with ADHD symptomology and cortical morphology in a population-based sample of adolescents.

Methods: Data were obtained from the IMAGEN study, which includes 2,223 adolescents. While undergoing functional imaging, participants passively viewed video clips of a face that started from a neutral expression and progressively turned angry, or, instead, turned to a second neutral expression. Left and right amygdala ROIs were used to extract mean BOLD signal from the angry face minus neutral face contrast for all subjects. T1-weighted images were processed through the CIVET pipeline (version 2.1.0). ADHD symptomatology was assessed using the Development and Well-Being Assessment, and Strengths and Difficulties Questionnaire.

Results: Youths exhibiting increased left amygdalar activation (+1.5 SDs) (92 participants; 40 females) possessed significantly greater parent- and self-reported ADHD symptomatology relative to all other subjects (p = .012-.038). Compared to the rest of the sample, youths exhibiting increased left amygdalar activation did not differ with regard to demographic variables, or other forms of psychopathology, including mood/anxiety symptoms. Increased amygdalar activation was associated with reduced cortical thickness in orbital/ventromedial prefrontal regions. Further analysis revealed significant negative associations between parent-reported ADHD symptoms and thickness in orbital/ventromedial prefrontal corticesdcortical thickness in these regions was negatively correlated with left amygdalar activation.

Conclusions: These findings suggest that cortico-amygdalar circuitry may underpin aspects of core ADHD symptomatology, not simply co-occurring mood and anxiety problems

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Biol Psychiatry. 2018;83:S83.

FROM MILLISECONDS TO YEARS IN ATTENTION DEFICIT HYPERACTIVITY DISORDER.

Shaw P, Sudre G.

Background: We consider how mapping neural activity in the order of milliseconds (the temporal microscale) can throw insights into processes pertinent to attention deficit hyperactivity disorder that have unfolded over years (the temporal macroscale). Specifically, we demonstrate how the degree of persistence into adulthood of childhood symptoms of inattention and hyperactivity/impulsivity is associated with patterns of adult neural activity.

Methods: 220 children had the course of their symptoms of inattention and hyperactivity/impulsivity assessed repeatedly into early adulthood. In adulthood, all had multimodal imaging (fMRI and magnetoencephalography- MEG) during both task of response inhibition and task free processing.

Results: The severity of symptoms persisting from childhood were tied to anomalies in functional connectivity, defined both electrophysiologically (using MEG) and hemodynamically (using fMRI), during task free and task dependent processing. All reported symptom-function associations reported survived adjustment for multiple testing through false discovery or Bonferroni procedures (adjusted alpha of 0.05). Adults whose symptoms had remitted showed neural activation patterns that did not differ significantly from individuals who were never affected. By contrast, adults with persistent symptoms differed significantly from those never affected, particularly in brain regions supporting response inhibition, and in the connectivity between the default mode network and networks supporting attention.

Conclusions: We find that adults whose ADHD symptoms have resolved since childhood do not differ from their neveraffected peers both neuro-electrophysiologically and hemodynamically. This is compatible with a model that holds remission occurring over year might be underpinned by a normalization of early anomalies of cortical dysfunction

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Biol Psychiatry. 2018;83:S152.

ADHD AND THE CORTEX: EVIDENCE FROM LARGE CLINICAL AND POPULATION BASED SAMPLES.

Hoogman M, Muetzel R, Shumskaya E, et al.

Background: Neuroimaging studies show structural alterations of various brain regions in children and adults with ADHD. However, these studies are often underpowered and heterogeneous in their methods. Here, we present data from large-scale clinical and population-based samples to study links between ADHD and the cortex.

Methods: For 2259 cases and 1938 controls (ENIGMA-ADHD) and 2707 children (Generation-R) cortical thickness and surface area of 34 regions was calculated (Desikan-Killiany atlas). Case-control differences in children, adolescents and adults were assessed, and effects of clinical measures (e.g. comorbidity) were studied. In the Generation-R sample, the association between cortical measures and CBCL-scores (attention/ ADHD) was analyzed. Also, familial effects on the cortex were studied.

Results: Children with ADHD showed smaller surface area values in various regions of the brain (e.g. total surface area, d= -0.25, pFDR=2.21E-07). Thickness of fusiform gyrus and temporal pole (both d=-0.22, pFDR=1.2E-07) were thinner in ADHD children versus controls. No differences in adolescents/ adulthood, and a limited contribution of clinical features were found. In Generation-R, CBCL-scores were associated with clinically-affected surface area values, pFDRE<0.05. Familial effects were found for total and lateralorbitofrontal surface area, and fusiform thickness.

Conclusions: Only children, but not adolescents and adults with ADHD had reduced surface area (global) and cortical thickness (temporal lobe). Surface area abnormalities were also associated with ADHD traits in a normal pediatric population. Our population and familiality analyses indicate a familial, either genetic or environmental, nature of these differences; they do not seem to be a mere consequence of living with ADHD

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Biol Psychiatry. 2018;83:S257.

INVESTIGATING THE EFFECT OF GLUTAMATE ON EXECUTIVE FUNCTIONS IN CHILDREN WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER USING MAGNETIC RESONANCE SPECTROSCOPY.

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

Background: Attention-deficit/hyperactivity disorder (ADHD) is a neurodevelopmental disorder in children, with a prevalence of 5-7%. Symptoms include inattention, impulsivity and hyperactivity. Previous studies have reported dysfunction in the glutamatergic pathway. However, no studies to date have linked the glutamate differences with performance in Executive Function (EF) tasks.
Methods: 31 children with ADHD (M = 10.2 years, SD = 1.3; males = 19) and 15 control participants (HC; M = 10.0 years, SD = 1.4 years; males = 6) took part. Short echo proton magnetic resonance spectroscopy (1H-MRS; TE = 30ms) were used to study the changes in in the right prefrontal cortex (R-PFC) and left striatum (LS). Both groups completed an EF assessment battery, Digit Span (DSB), Letter Fluency (LF) and Trail Making TestePart B, (TMT-B).
Results: Independent t-tests found lower concentrations of Glutamate (Glu; p = 0.009), Choline (Cho; p = 0.016) and NAcetyl Aspartate (NAA; p = 0.029) in the R-PFC in ADHD participants compared to HC. No significant differences were seen in the LS. Positive correlation with Glu concentration and performance in DSB, LF and TMTB tasks in the control group were observed. No such correlations were observed in the ADHD group.
Conclusions: To our knowledge, this is the first study to investigate the relationship between EF and Glu concentration. These findings suggest the decoupling effect of Glu in EF related tasks in children with ADHD compared to controls. As such, Glu concentration can be a possible ADHD biomarker and the RPFC can be a novel treatment target for future

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Biol Psychiatry. 2018;83:S84.

COGNITIVE AND NEUROIMAGING APPROACHES TO UNCOVERING THE TEMPORAL ARCHITECTURE OF ADHD.

Durston S, Ambrosino S, Van BJ, et al.

Background: Temporal dynamics are particularly relevant to ADHD, at both the Micro- and the Macro-level. At the Microlevel, the most robust finding for cognitive changes in ADHD is for moment-to-moment variability in response timing on cognitive tasks, whereas at the Macro-level, changes in brain structure with development have been tied to clinically relevant measures, such as outcome and stimulus treatment. I will consider how individual differences in reactivity in ADHD and ASD (micro-level) and longitudinal data on the temporal dynamics of development (macro-level) may inform us on underlying psychopathological mechanisms.
Methods: Cognitive data were collected from 405 children with ADHD, ASD & TD. Ex-Gaussian distribution parameters were used to characterize intra-individual variability on fast and slow responses. Longitudinal measures of brain development were collected for children with ADHD and controls.
Results: We found higher variability on both fast and slow responses for children with ADHD and ASD ($p < .05$). For children with ASD, variability remained high over development, whereas for children with ADHD it decreased at a rate similar to controls. Similarly, we found widespread reductions in cortical surface area and gyrification in ADHD that were stable over development ($p < .05$).
Conclusions: I will discuss how differences in response variability give insights into shared and unique mechanisms across ADHD and ASD. Additionally, I consider how measures of brain anatomy can inform us on early developmental mechanisms. These findings will be contrasted to those on mood disorders also discussed in the symposium

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Biol Psychiatry. 2018;83:S158-S159.

AUTOMATED RECONSTRUCTION OF WHITE MATTER PATHWAYS IN ATTENTION-DEFICIT/HYPERACTIVITY DISORDER USING ANATOMICAL PRIORS.

Damatac CG, Zwiers M, Franke B, et al.

Background: ADHD has repeatedly been associated with alterations in white matter microstructure, as measured through fractional anisotropy (FA) and acquired through diffusionweighted MRI (DWI). Due to methodological heterogeneity of analysis techniques, there have been inconsistent results regarding anatomical specificity of changes in FA. The aim of this study was to determine, in an automated manner, whether FA is related to ADHD in a large cohort of patients and healthy controls.
Methods: A cross-sectional analysis was performed on DWI data collected from 592 adolescents (285 unaffected, 247 affected, 60 subthreshold; mean age = 16.97 years) from the NeuroIMAGE study. Eighteen major white matter pathways in each subject were automatically segmented using TRACULA, a tractography toolbox within Freesurfer. We applied a mixed model regression to test for overall FA differences between groups. To explore tract-specific effects, linear regression was applied for each of the 18 tracts separately.
Results: No significant differences were found for overall, global FA between subject groups. A nominally significant difference in FA between groups was observed in the right corticospinal tract (rCST) [$F(2, 581) = 3.017$; $p = 0.04972$, uncorrected]. No other white matter pathways resulted in a significant difference between groups, and there was no effect of age and gender.
Conclusions: This tractography analysis in a large sample indicates no prominent changes in FA associated with ADHD diagnosis in adolescence. Nevertheless, our results are consistent with previous findings that suggest that FA in the CST is related to changes in hyperactive/impulsive symptoms

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Biol Psychiatry. 2018;83:S154-S155.

IS INCREASED RESPONSE TIME VARIABILITY RELATED TO DEFICIENT EMOTIONAL SELF-REGULATION IN CHILDREN WITH ADHD?

Elmaghrabi S, Nahmias M, Adamo N, et al.

Background: Elevated reaction time intra-subject variability (RT-ISV) characterizes Attention-Deficit/Hyperactivity Disorder (ADHD). Deficient emotional self-regulation (DESR), defined by adding Child Behavior Checklist Anxious/Depressed, Aggressive Behavior, and Attention Problems subscale scores, has been associated with worse outcome in ADHD. To determine if DESR is differentially associated with elevated RT-ISV, we examined RT-ISV in children with ADHD with and without DESR and in typically developing children (TDC). If DESR were related to increased RT-ISV, the latter could be used as a neuropsychological marker to help identify children with ADHD at higher risk for poor outcome, with potential clinical value.
Methods: We contrasted RT-ISV during a 6-min Eriksen Flanker Task in 31 children with ADHD without DESR, 34 with ADHD with DESR, and 65 TDC. Mean response time, RT standard deviation, RT coefficient of variation, and ex- Gaussian parameters were computed for each subject.
Results: Regardless of DESR, children with ADHD showed significantly greater RT-ISV than TDC ($p<0.001$). The two ADHD subgroups, defined by presence or absence of DESR, did not differ from each other.
Conclusions: Increased RT-ISV characterizes ADHD regardless of comorbid DESR. Along with a similar finding in adults with ADHD, these results suggest that RT-ISV is domainspecific rather than domain-general, I.e., related to cognitive rather than emotional dysregulation in ADHD

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Biol Psychiatry. 2018;83:S23.

UNIQUE NEURAL ASSOCIATIONS WITH PEDIATRIC IRRITABILITY DURING FRUSTRATION AND THREAT ORIENTING.

Leibenluft E, Tseng W-L, Kircanski K, et al.

Background: Irritability, defined as increased proneness to anger relative to peers, is extremely common in youth, yet there are few evidence-based treatments. Elucidating the relevant circuitry dysfunction would facilitate the development of mechanism-based interventions. We have posited two core deficits in irritability:

aberrant responses to frustration (i.e., blocked goal attainment) and aberrant approach responses to threat. We present data from two fMRI studies, a frustration task and a threat orienting task.
Methods: For both studies, phenotyping consisted of dimensional measures of parent- and child-reported irritability and anxiety, and parent-reported ADHD. Whole-brain corrected analyses identified findings unique to irritability and to anxiety, while covarying effects of ADHD. The frustration study included 195 youth (severe impairing irritability (DSM-5 DMDD, n=52), anxiety (n=42), and/or ADHD (n=40), and healthy volunteers (HV, n=61). This was a cued-attention orienting task with reward contingencies that were rigged to induce frustration. The threat orienting study included 197 youth (DMDD=54, anxiety=50, ADHD=37, HV=56). Bifactor modeling differentiated unique and shared effects of irritability and anxiety.
Results: For the frustration task, on trials where subjects performed the attention orienting task following frustration, irritability was positively associated with fronto-striatal activation (r's=.31-.39, p's<.05). When subjects attended away from threat, higher parent-reported irritability was associated with increased activity in the amygdala ROI (t189=2.30, p=.022), insula, caudate, and ventrolateral and dorsolateral prefrontal cortex (ts189>4.15, ps<.001). Higher anxiety was associated with decreased amygdala connectivity to cingulate and thalamus (ts189<-4.19, ps<.001).
Conclusions: Unique neural associations with irritability during frustration and threat orienting that could serve as potential biomarkers and treatment targets

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Biol Psychiatry. 2018;83:S153.

PARSING ATTENTION DYSFUNCTION IN CHILDREN WITH AUTISM SPECTRUM DISORDER AND ATTENTION DEFICIT/HYPERACTIVITY DISORDER.

Nattel S, Wilkinson E, Kristin M, et al.

Background: Autism spectrum disorder (ASD) and attention deficit/hyperactivity disorder (ADHD) frequently co-occur. One approach to study this comorbidity, is through the exploration of convergent symptoms. Aberrant attention, a core feature of ADHD, is widely present in ASD. Despite evidence of aberrant attention in ASD, the underlying mechanism/s and its correlation to ADHD is poorly understood.
Methods: Sixteen children with ASD (mean age 8.3, SD 1.3) were included in this study. All children met DSM-5 criteria for ASD. In addition, all participants were evaluated for ADHD. Standardized measures of cognitive and adaptive functioning were obtained. Parents completed the Swanson Nolan and Pelham Questionnaire (SNAP) and Child Behavior Checklist (CBCL). Finally, all children completed the Attention Network Test (ANT) and a gap-overlap eye-tracking paradigm.
Results: Half of the participants met diagnostic criteria for ADHD. There was no difference in baseline demographic factors. Children with comorbid ADHD performed worse on VABS-2 (p=0.03). Neither the SNAP nor the CBCL captured symptoms of ADHD accurately. Nonetheless, statistical differences in subscales suggestive of hyperactivity were noted (all p<0.01). Statistical differences in the ANT for the orienting (F(2,13)=18.82, p=0.0001) and executive (F(2,13)=4.60, p=0.0308) networks were found. Finally, individual social disengagement times were inversely correlated to adaptive scores.
Conclusions: Our results suggest that commonly used clinical instruments might prove deficient when assessing for ADHD in children with ASD. Objective measures of attention, as the ANT and eye-tracking, are alternatives that might offer important insights into the nature of this comorbidity

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Biological Psychiatry: Cognitive Neuroscience and Neuroimaging. 2018.

FRONTOSTRIATAL DYSFUNCTION DURING DECISION MAKING IN ATTENTION-DEFICIT/HYPERACTIVITY DISORDER AND OBSESSIVE-COMPULSIVE DISORDER.

Norman LJ, Carlisi CO, Christakou A, et al.

Background: The aim of the current paper is to provide the first comparison of computational mechanisms and neurofunctional substrates in adolescents with attention-deficit/hyperactivity disorder (ADHD) and adolescents with obsessive-compulsive disorder (OCD) during decision making under ambiguity.

Methods: Sixteen boys with ADHD, 20 boys with OCD, and 20 matched control subjects (12ΓÇô18 years of age) completed a functional magnetic resonance imaging version of the Iowa Gambling Task. Brain activation was compared between groups using three-way analysis of covariance. Hierarchical Bayesian analysis was used to compare computational modeling parameters between groups.
Results: Patient groups shared reduced choice consistency and relied less on reinforcement learning during decision making relative to control subjects, while adolescents with ADHD alone demonstrated increased reward sensitivity. During advantageous choices, both disorders shared underactivation in ventral striatum, while OCD patients showed disorder-specific underactivation in the ventromedial orbitofrontal cortex. During outcome evaluation, shared underactivation to losses in patients relative to control subjects was found in the medial prefrontal cortex and shared underactivation to wins was found in the left putamen/caudate. ADHD boys showed disorder-specific dysfunction in the right putamen/caudate, which was activated more to losses in patients with ADHD but more to wins in control subjects.
Conclusions: The findings suggest shared deficits in using learned reward expectancies to guide decision making, as well as shared dysfunction in medio-fronto-striato-limbic brain regions. However, findings of unique dysfunction in the ventromedial orbitofrontal cortex in OCD and in the right putamen in ADHD indicate additional, disorder-specific abnormalities and extend similar findings from inhibitory control tasks in the disorders to the domain of decision making under ambiguity

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Biological Psychiatry: Cognitive Neuroscience and Neuroimaging. 2018.
A NETWORK NEUROSCIENCE APPROACH TO TYPICAL AND ATYPICAL BRAIN DEVELOPMENT.
Morgan SE, White SR, Bullmore ET, et al.
Human brain networks based on neuroimaging data have already proven useful in characterizing both normal and abnormal brain structure and function. However, many brain disorders are neurodevelopmental in origin, highlighting the need to go beyond characterizing brain organization in terms of static networks. Here, we review the fast-growing literature shedding light on developmental changes in network phenotypes. We begin with an overview of recent large-scale efforts to map healthy brain development, and we describe the key role played by longitudinal data including repeated measurements over a long period of follow-up. We also discuss the subtle ways in which healthy brain network development can inform our understanding of disorders, including work bridging the gap between macroscopic neuroimaging results and the microscopic level. Finally, we turn to studies of three specific neurodevelopmental disorders that first manifest primarily in childhood and adolescence/early adulthood, namely psychotic disorders, attention-deficit/hyperactivity disorder, and autism spectrum disorder. In each case we discuss recent progress in understanding the atypical features of brain network development associated with the disorder, and we conclude the review with some suggestions for future directions

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Brain Imaging Behav. 2018;1-9.
PRELIMINARY EVIDENCE OF ALTERED GRAY MATTER VOLUME IN SUBJECTS WITH INTERNET GAMING DISORDER: ASSOCIATIONS WITH HISTORY OF CHILDHOOD ATTENTION-DEFICIT/HYPERACTIVITY DISORDER SYMPTOMS.
Lee D, Namkoong K, Lee J, et al.
Attention-deficit/hyperactivity disorder (ADHD) is commonly comorbid with Internet gaming disorder (IGD). Although childhood ADHD symptoms may decline during late brain maturation, structural alterations in some brain areas may persist into adulthood. This study investigated whether young adults with IGD and a history of childhood ADHD symptoms had gray matter volume (GMV) alterations that were distinct from subjects without a history of childhood ADHD. As an exploratory investigation, we conducted a whole-brain voxel-based morphometry with the diffeomorphic anatomical registration using an exponentiated Lie algebra algorithm and applied an uncorrected threshold at the voxel level for multiple comparisons. GMVs of IGD subjects with a history of childhood ADHD (IGDADHD+ group; n = 20; 24.5 -¦ 2.5 years) were compared to those of subjects without a history of childhood ADHD (IGDADHD- group; n = 20; 23.9 -¦ 2.5 years) and controls (n = 20; 22.7 -¦ 2.4 years). Compared with controls, both IGD groups had a smaller GMV in the right

anterior cingulate cortex, the left inferior frontal gyrus, and the left insula, yet had a larger GMV in the right angular gyrus. The IGDADHD+ group had a larger GMV in the right precuneus than the IGDADHD- group and controls. When controlling for other comorbid psychiatric symptoms, the IGDADHD+ group also had a smaller GMV in the right inferior frontal gyrus. In conclusion, we found that young adults with IGD and a history of childhood ADHD symptoms had characteristic GMV alterations, which may be linked with their manifestation of childhood ADHD

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Brain Imaging Behav. 2018;12:499-508.

IMPAIRED ENGAGEMENT OF THE VENTRAL ATTENTION SYSTEM IN NEUROFIBROMATOSIS TYPE 1.

Pride NA, Korgaonkar MS, North KN, et al.

Individuals with neurofibromatosis type 1 (NF1) exhibit significant impairments in attention across multiple domains. Very little is known about the contributing neural networks. We used task-based functional magnetic resonance imaging (fMRI) to examine dorsal and ventral attention networks during auditory oddball processing in children and adolescents with NF1 and typically developing controls. Significant differences in neural activation patterns were identified within brain regions supporting the ventral attention system. Children with NF1 demonstrated hypoactivation in the temporoparietal junction and the anterior cingulate cortex compared to typically developing children. Hypoactivation in the anterior cingulate cortex was associated with poorer selective attention and attentional control in children with NF1. Results indicate an abnormality in bottom-up attention networks in NF1 that may lead to inefficient and faulty suppression of stimulus-driven information outside the current attentional set that play a significant role in the NF1 behavioral phenotype

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Child Dev. 2018 Mar;89:509-24.

PEER PROBLEMS AND HYPERACTIVITY–IMPULSIVITY AMONG NORWEGIAN AND AMERICAN CHILDREN: THE ROLE OF 5-HTTLPR.

Stenseng F, Li Z, Belsky J, et al.

Peer problems are linked to attention deficit hyperactivity disorder (ADHD) symptoms and the serotonin system is thought to be involved in ADHD-related behavior. Hence, from a Gene × Environment perspective, the serotonin transporter 5-HTTLPR may play a moderating role. In two large community samples, the moderating role of 5-HTTLPR was examined related to more hyperactivity–impulsivity symptoms (HI symptoms) predicted by more peer problems. In Study 1, involving 642 Norwegian children, results indicated that for s-allele carriers only, caregiver-reported peer problems at age 4 predicted more parent-reported HI symptoms at age 6. In Study 2, similar results emerged involving 482 American children. Discussion focuses on differential sensitivity to the adverse effects of poor peer relations

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Clin Neuropharmacol. 2018 Mar;41:82-83.

TREATMENT OF INTERMITTENT EXPLOSIVE DISORDER WITH CARBAMAZEPINE.

Coskun F, Akca OF.

The goal in this case report is to present an adolescent case with ADHD and Intermittent explosive disorder (IED) showing dramatic improvements with carbamazepine treatment despite not responding to various other pharmacological agents. Intermittent explosive disorder (IED) is an impulse-control disorder (ICD) defined by recurrent verbal or physical aggressive episodes that are nonproportional to psychosocial stressors or provocation. Physical or verbal aggressive episodes mostly begin abruptly with or without psychosocial stressors, last for a short period, and often lead to social, professional, legal, and financial problems. Anger outbursts usually start with a small triggering event concerning a close friend, colleague, or partner, although the triggering event may not be identified in many cases. The IED frequency was 3% to 5% in an epidemiological study that included adults and adolescents. Intermittent explosive disorder is more common

in males and usually begins in late adolescence. Intermittent explosive disorder is also more common in individuals with attention-deficit/hyperactivity disorder (ADHD)

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Clin Neuropsychiatry. 2018;15:123-31.

ADULTS WITH ADHD A RETROSPECTIVE ACCOUNT OF THE FAMILY SYSTEMS AND ATTACHMENT RELATIONSHIPS.

Syrjänen M, Hautamäki A, Pleshkova N, et al.

Objective: This multiple-case study explores the self-protective attachment strategies of adults with ADHD and the history of the dangers in their family of origin.

Method: Nine respondents were interviewed using the Adult Attachment Interview, AAI (The Dynamic Maturational Model modification).

Results: All respondents had experienced dangers connected to the lack of protection and comfort in their families of origin, including unresolved traumas, such as early emotional neglect, later supervision neglect, abuse and witnessing discord, even domestic violence, in triangulated family relationships. Three subgroups were formed on the basis of the attachment classifications.

Conclusions: The recognition of the variety of attachment strategies, disorientation modifying, and unresolved traumas interrupting the strategic self-protective functioning, can contribute to the tailoring of individualized psychological treatment. The psychological treatment would help these adults with ADHD to understand how the unresolved traumas and triangulated family systems have impacted and still impact them

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Dev Med Child Neurol. 2018.

QUALITY OF LIFE AND PSYCHOSOCIAL FUNCTIONING IN ADOLESCENTS WITH DEVELOPMENTAL COORDINATION DISORDER AND ATTENTION-DEFICIT-HYPERACTIVITY DISORDER.

Cairney J.

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Dev Neurorehabilitation. 2018;1-6.

VIRTUAL REALITY TRAINING TO ENHANCE BEHAVIOR AND COGNITIVE FUNCTION AMONG CHILDREN WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER: BRIEF REPORT.

Shema-Shiratzky S, Brozgol M, Cornejo-Thumm P, et al.

Purpose: To examine the feasibility and efficacy of a combined motor-cognitive training using virtual reality to enhance behavior, cognitive function and dual-tasking in children with Attention-Deficit/Hyperactivity Disorder (ADHD).

Methods: Fourteen non-medicated school-aged children with ADHD, received 18 training sessions during 6-áweeks. Training included walking on a treadmill while negotiating virtual obstacles. Behavioral symptoms, cognition and gait were tested before and after the training and at 6-weeks follow-up.

Results: Based on parental report, there was a significant improvement in children's social problems and psychosomatic behavior after the training. Executive function and memory were improved post-training while attention was unchanged. Gait regularity significantly increased during dual-task walking. Long-term training effects were maintained in memory and executive function.

Conclusion: Treadmill-training augmented with virtual-reality is feasible and may be an effective treatment to enhance behavior, cognitive function and dual-tasking in children with ADHD

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Environ Health Perspect. 2018;126:057004-1.

PRENATAL PHTHALATES, MATERNAL THYROID FUNCTION, AND RISK OF ATTENTION-DEFICIT HYPERACTIVITY DISORDER IN THE NORWEGIAN MOTHER AND CHILD COHORT.

Engel SM, Villanger GD, Nethery RC, et al.

BACKGROUND: There is growing concern that phthalate exposures may have an impact on child neurodevelopment. Prenatal exposure to phthalates has been linked with externalizing behaviors and executive functioning defects suggestive of an attentiondeficit hyperactivity disorder (ADHD) phenotype.
OBJECTIVES: We undertook an investigation into whether prenatal exposure to phthalates was associated with clinically confirmed ADHD in a population-based nested case - control study of the Norwegian Mother and Child Cohort (MoBa) between the years 2003 and 2008.
METHODS: Phthalate metabolites were measured in maternal urine collected at midpregnancy. Cases of ADHD (n = 297) were obtained through linkage between MoBa and the Norwegian National Patient Registry. A random sample of controls (n = 553) from the MoBa population was obtained. RESULTS: In multivariable adjusted coexposure models, the sum of di-2-ethylhexyl phthalate metabolites (+ú DEHP) was associated with a monotonically increasing risk of ADHD. Children of mothers in the highest quintile of +ú DEHP had almost three times the odds of an ADHD diagnosis as those in the lowest [OR = 2: 99 (95% CI: 1.47, 5.49)]. When +ú DEHP was modeled as a log-linear (natural log) term, for each log-unit increase in exposure, the odds of ADHD increased by 47% [OR = 1: 47 (95% CI: 1.09, 1.94)]. We detected no significant modification by sex or mediation by prenatal maternal thyroid function or by preterm delivery.
CONCLUSIONS: In this population-based case - control study of clinical ADHD, maternal urinary concentrations of DEHP were monotonically associated with increased risk of ADHD. Additional research is needed to evaluate potential mechanisms linking phthalates to ADHD

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Eur Child Adolesc Psychiatry. 2018 Mar;27:267-77.

ADHD IS ASSOCIATED WITH MIGRAINE: A SYSTEMATIC REVIEW AND META-ANALYSIS.

Salem H, Vivas D, Cao F, et al.

An association between primary headaches and attention-deficit/hyperactivity disorder (ADHD) has long been suggested. Moreover, headache is regarded as a common side effect of stimulants, the most effective treatment for ADHD. So far, no systematic review has evaluated the potential association between ADHD and headache. We performed a systematic review of the literature and a meta-analysis of all reported studies on ADHD and primary headaches. Our analysis showed a positive association between ADHD and migraine (OR 1.322, 95% CI 1.018-1717, p value 0.036), but not with tension-type headache. There is a significant association between migraine and ADHD. The mechanisms underlying this association remain to be elucidated, warranting further studies

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Eur Child Adolesc Psychiatry. 2018;27:663-75.

ASSOCIATIONS BETWEEN ATTENTION-DEFICIT/HYPERACTIVITY DISORDER AND AUTOIMMUNE DISEASES ARE MODIFIED BY SEX: A POPULATION-BASED CROSS-SECTIONAL STUDY.

Hegvik T-A, Instanes JT, Haavik J, et al.

Several studies have demonstrated associations between neuropsychiatric disorders, such as attention-deficit/hyperactivity disorder (ADHD), and the immune system, including autoimmune diseases. Since ADHD and many autoimmune diseases show sex-specific properties, such associations may also differ by sex. Using Norwegian national registries, we performed a cross-sectional study based on a cohort of 2,500,118 individuals to investigate whether ADHD is associated with common autoimmune diseases. Associations between ADHD and autoimmune diseases in females and males were investigated with logistic regression and effect modification by sex was evaluated. Several subanalyses were performed. The strongest association was found between ADHD and psoriasis in females, adjusted odds ratio (adjOR)-á=-á1.57 (95% confidence interval: 1.46ΓÇô1.68) and males, adjOR-á=-á1.31 (1.23ΓÇô1.40); p value for interaction-á<-á0.0001. Furthermore, among females, ADHD was associated with CrohnΓÇÖs disease, adjOR-á=-á1.44

(1.16-1.79) and ulcerative colitis, adjOR-á=-á1.28 (1.06-1.54). In contrast, males with ADHD had lower odds of CrohnΓÇÖs disease, adjOR-á=-á0.71 (0.54-0.92), in addition to a trend for lower odds of ulcerative colitis, adjOR-á=-á0.86 (0.71-1.03); p values for interaction-á<-á0.0001 and 0.0023, respectively. In a group of females where information on smoking and body mass index was available, adjustment for these potential mediators did not substantially alter the associations. Our findings support previously reported associations between ADHD and diseases of the immune system. The associations differ by sex, suggesting that sex-specific immune-mediated neurodevelopmental processes may be involved in the etiology of ADHD

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Eur Child Adolesc Psychiatry. 2018;1-3.

DIFFERENTIATING BETWEEN ADHD AND ASD IN CHILDHOOD: SOME DIRECTIONS FOR PRACTITIONERS.

Rommelse N, Visser J, Hartman C.

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Front Psychiatry. 2018;9.

LEG MOVEMENT ACTIVITY DURING SLEEP IN ADULTS WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.

Garbazza C, Sauter C, Paul J, et al.

Objectives: To conduct a first detailed analysis of the pattern of leg movement (LM) activity during sleep in adult subjects with Attention-Deficit/Hyperactivity Disorder (ADHD) compared to healthy controls.

Methods: Fifteen ADHD patients and 18 control subjects underwent an in-lab polysomnographic sleep study. The periodic character of LMs was evaluated with established markers of "periodicity," i.e., the periodicity index, intermovement intervals, and time distribution of LM during sleep, in addition to standard parameters such as the periodic leg movement during sleep index (PLMSI) and the periodic leg movement during sleep arousal index (PLMSAI). Subjective sleep and psychiatric symptoms were assessed using several, self-administered, screening questionnaires.

Results: Objective sleep parameters from the baseline night did not significantly differ between ADHD and control subjects, except for a longer sleep latency (SL), a longer duration of the periodic leg movements during sleep (PLMS) in REM sleep and a higher PLMSI also in REM sleep. Data from the sleep questionnaires showed perception of poor sleep quality in ADHD patients.

Conclusions: Leg movements during sleep in ADHD adults are not significantly more frequent than in healthy controls and the nocturnal motor events do not show an increased periodicity in these patients. The non-periodic character of LMs in ADHD has already been shown in children and seems to differentiate ADHD from other pathophysiological related conditions like restless legs syndrome (RLS) or periodic limb movement disorder (PLMD). The reduced subjective sleep quality reported by ADHD adults contrasted with the normal objective polysomnographic parameters, which could suggest a sleep-state misperception in these individuals or more subtle sleep abnormalities not picked up by the traditional sleep staging

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Hum Brain Mapp. 2018.

VISUAL PROCESSING AS A POTENTIAL ENDOPHENOTYPE IN YOUTHS WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER: A SIBLING STUDY DESIGN USING THE COUNTING STROOP FUNCTIONAL MRI.

Fan L-Y, Shang C-Y, Tseng W-Y, et al.

Deficits in inhibitory control and visual processing are common in youths with attention-deficit/hyperactivity disorder (ADHD), but little is known about endophenotypes for unaffected siblings of youths with ADHD. This study aimed to investigate the potential endophenotypes of brain activation and performance in inhibitory control and visual processing among ADHD probands, their unaffected siblings, and neurotypical youths. We assessed 27 ADHD probands, 27 unaffected siblings, and 27 age-, gender-, and IQ-matched neurotypical youths using the counting Stroop functional magnetic resonance imaging and two tasks of the Cambridge Neuropsychological Test Automated Battery (CANTAB): rapid visual information processing (RVP) for inhibitory control and spatial span (SSP) for visual processing. ADHD probands showed greater activation

than their unaffected siblings and neurotypical youths in the right inferior frontal gyrus (IFG) and anterior cingulate cortex. Increased activation in the right IFG was positively correlated with the mean latency of the RVP in ADHD probands. Moreover, ADHD probands and their unaffected siblings showed less activation in the left superior parietal lobule (SPL) than neurotypical youths. Increased activation in the left SPL was positively correlated with the spatial length of the SSP in neurotypical youths. Our findings suggest that less activation in the left SPL might be considered as a candidate imaging endophenotype for visual processing in ADHD

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Hum Brain Mapp. 2018;39:2442-54.

LOCAL FUNCTIONAL CONNECTIVITY SUGGESTS FUNCTIONAL IMMATURITY IN CHILDREN WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.

Marcos-Vidal L, Mart+¡nez-Garc+¡a M, Pretus C, et al.

Previous studies have associated Attention-Deficit/Hyperactivity Disorder (ADHD) with a maturational lag of brain functional networks. Functional connectivity of the human brain changes from primarily local to more distant connectivity patterns during typical development. Under the maturational lag hypothesis, we expect children with ADHD to exhibit increased local connectivity and decreased distant connectivity compared with neurotypically developing (ND) children. We applied a graph-theory method to compute local and distant connectivity levels and cross-sectionally compared them in a sample of 120 children with ADHD and 120 age-matched ND children (age range = 7ΓÇô17 years). In addition, we measured if potential group differences in local and distant connectivity were stable across the age range considered. Finally, we assessed the clinical relevance of observed group differences by correlating the connectivity levels and ADHD symptoms severity separately for each group. Children with ADHD exhibited more local connectivity than age-matched ND children in multiple brain regions, mainly overlapping with default mode, fronto-parietal and ventral attentional functional networks (p <.05- threshold free-cluster enhancement-family-wise error). We detected an atypical developmental pattern of local connectivity in somatomotor regions, that is, decreases with age in ND children, and increases with age in children with ADHD. Furthermore, local connectivity within somatomotor areas correlated positively with clinical severity of ADHD symptoms, both in ADHD and ND children. Results suggest an immature functional state of multiple brain networks in children with ADHD. Whereas the ADHD diagnosis is associated with the integrity of the system comprising the fronto-parietal, default mode and ventral attentional networks, the severity of clinical symptoms is related to atypical functional connectivity within somatomotor areas. Additionally, our findings are in line with the view of ADHD as a disorder of deviated maturational trajectories, mainly affecting somatomotor areas, rather than delays that normalize with age

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INDIAN JOURNAL OF OTOLOGY. 2017;23:244-46.

OPTIMIZING OUTCOMES IN PEDIATRIC COCHLEAR IMPLANT RECIPIENTS WITH COEXISTING ATTENTION DEFICIT HYPERACTIVE DISORDER.

Mittal R, Raj P.

Introduction: Speech language outcomes are often variable in hearing impaired children managed with cochlear Implantation. Co-existing Attention Deficit Hyperactive Disorder may be responsible in some cases. Active management of these cases may result in improved outcomes in terms of better speech language acquisition. This study compared the progress in speech language acquisition in paediatric cochlear implant recipients with coexisting ADHD before and after intervention with Behaviour Modification Therapy (BMT) and /or pharmacological treatment.

Materials and Methods: The study group was of 20 hearing impaired children post cochlear implant with co-existing ADHD who did not show expected results with regular AVT for 3 months post implant. Management of ADHD was instituted as per laid down protocol and CAP scores were compared at 0, 3, 6, 9 and 12 months post implantation. The scores obtained were subjected to a Wilcoxon sign rank test and P value derived.

Results: The CAP scores after the inclusion of treatment for ADHD showed a definite improvement with a highly significant P value.
Conclusions: Variables such as co-existent ADHD must be actively looked for in hearing impaired children prior to surgery and. Appropriate treatment in the form of BMT and / or medication should be instituted to improve the performance

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Ir J Psychol Med. 2018;1-4.
ADHD: SCIENCE, STIGMA AND SERVICE IMPLICATIONS.
Gavin B, McNicholas F.
We are delighted to dedicate an edition of the Irish Journal of Psychological Medicine to the topic of attention-deficit hyperactivity disorder (ADHD). ADHD accounts for the majority of clinical presentations to Child and Adolescent Mental Health Services, both in terms of new assessments and ongoing attendances. Papers presented in this edition reflect on the evolving construct of ADHD, drawing from science, clinical practice and public opinion. Current and evidenced-based assessment and treatment practice guidelines are reviewed. International longitudinal studies allow us to understand the personal and societal cost, which can persist for many years post-diagnosis. Despite continuation to adulthood in many young people, follow on adult services are lacking. It is fitting that submissions, by way of personal reflections and opinion pieces, are also included from adult colleagues as they reflect on their experiences in this area. Given the recent development of a national clinical programme in ADHD in Ireland, coupled with a growing evidence for effective interventions, it is hoped that this special edition will highlight the need for appropriate and accessible ADHD treatments across the lifespan

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Ir J Psychol Med. 2018;1-5.
ARE THE EFFECTS OF METHYLPHENIDATE UNCERTAIN?
Cortese S.
Objectives: A recent systematic review and meta-analysis of randomised controlled trials of methylphenidate (MPH) in children and adolescents by a Cochrane group, led by Storeb©, raised concern around the level of evidence supporting the use of this medication for attention-deficit/hyperactivity disorder (ADHD) in children and adolescents. This led to several critical responses from a number of ADHD experts.
Methods: This paper reviews the conclusions reached from the Storeb© meta-analysis by a critical analysis of methodologies used along with drawing on extant literature.
Results: The controversy raised by the Cochrane meta-analysis should lead to a balanced reflection on the research priorities and needs for the field.
Conclusions: It is hoped the controversy will ultimately lead to improve the quality of the research on the efficacy, effectiveness and tolerability of MPH for ADHD

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JAMA Pediatr. 2018;172:437-43.
SECONDARY ATTENTION-DEFICIT/HYPERACTIVITY DISORDER IN CHILDREN AND ADOLESCENTS 5 TO 10 YEARS AFTER TRAUMATIC BRAIN INJURY.
Narad ME, Kennelly M, Zhang N, et al.
IMPORTANCE After traumatic brain injury (TBI), children often experience impairment when faced with tasks and situations of increasing complexity. Studies have failed to consider the potential for attention problems to develop many years after TBI or factors that may predict the development of secondary attention-deficit/hyperactivity disorder (SADHD). Understanding these patterns will aid in timely identification of clinically significant problems and appropriate initiation of treatment with the hope of limiting additional functional impairment.

OBJECTIVE To examine the development of SADHD during the 5 to 10 years after TBI and individual (sex, age at injury, and injury characteristics) and environmental (socioeconomic status and family functioning) factors that may be associated with SADHD.
DESIGN, SETTING, AND PARTICIPANTS Concurrent cohort/prospective study of children aged 3 to 7 years hospitalized overnight for TBI or orthopedic injury (OI; used as control group) who were screened at 3 tertiary care children's hospitals and 1 general hospital in Ohio from January 2003 to June 2008. Parents completed assessments at baseline (0-3 months), 6 months, 12 months, 18 months, 3.4 years, and 6.8 years after injury. A total of 187 children and adolescents were included in the analyses: 81 in the TBI group and 106 in the OI group.
MAIN OUTCOMES AND MEASURES Diagnosis of SADHDwas the primary outcome. Assessments were all completed by parents. Secondary ADHD was defined as an elevated T score on the DSM-Oriented Attention-Deficit/Hyperactivity Problems Scale of the parent-reported Child Behavior Checklist, report of an ADHD diagnosis, and/or current treatment with stimulant medication not present at the baseline assessment. The Family Assessment Device-Global Functioning measurement was used to assess family functioning; scores ranged from 1 to 4, with greater scores indicating poorer family functioning.
RESULTS The analyzed sample included 187 children with no preinjury ADHD. Mean (SD) age was 5.1 (1.1) years; 108 (57.8%) were male, and 50 (26.7%) were of nonwhite race/ethnicity. Of the 187 children, 48 (25.7%) met our definition of SADHD. Severe TBI (hazard ratio [HR], 3.62; 95%CI, 1.59-8.26) was associated with SADHD compared with the OI group. Higher levels of maternal education (HR, 0.33; 95%CI, 0.17-0.62) were associated with a lower risk of SADHD. Family dysfunction was associated with increased risk of SADHD within the TBI group (HR, 4.24; 95%CI, 1.91-9.43), with minimal association within the OI group (HR, 1.32; 95%CI, 0.36-4.91).
CONCLUSIONS AND RELEVANCE Early childhood TBI was associated with increased risk for SADHD. This finding supports the need for postinjury monitoring for attention problems. Consideration of factors that may interact with injury characteristics, such as family functioning, will be important in planning clinical follow-up of children with TBI

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J Bras Psiquiatr. 2018;67:126-34.
INTERNET ADDICTION AND ATTENTION DEFICIT HYPERACTIVITY DISORDER (ADHD): INTEGRATIVE REVIEW OF THE LITERATURE.
Schmidek HCMV, Gomes JC, dos Santos PL, et al.
Objective: To perform an integrative review of the possible relationship between internet addiction (ID) and attention deficit hyperactivity disorder (ADHD) in adolescents aged 12 to 18 years. Also to gather informations in these studies for a more efficient diagnosis of DI.
Methods: Integrative review of the literature in three databases: PsycINFO, Scopus and Cinahal, with the following terms: internet addiction, adolescent and attention deficit disorder with hyperactivity, 2007-2017, with information about the relationship between Internet addiction and ADHD.
Results: The sample consisted of 12 original articles, mostly from Asia and the Middle East. From their analysis, the following categories emerged: Relationship between ID and ADHD; Other factors associated with ID; Instruments for evaluation of ID and incidence data. There is a lack of defined criteria for diagnosis of internet addiction, and four instruments were identified to measure ID, all questionnaires were completed by the adolescents themselves, with rates ranging from 2.4% to 10.6%. Anxiety and depression disorders were the most cited comorbidities after ADHD in the adolescents diagnosed with ID.
Conclusions: There are evidences of an important association between the two identified disorders, however without conclusive results on the interaction process. In order to establish therapeutic interventions and strategies to prevent the problem, it is necessary to advance research on the definition of the diagnostic criteria of ID, prevalence rates and predictors of the problem

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J Affective Disord. 2018;236:120-26.

DO MOTHERS WHO ARE ANXIOUS DURING PREGNANCY HAVE INATTENTIVE CHILDREN?

Bolea-Alamaac B, Davies SJ, Evans J, et al.

Background: Maternal somatic anxiety during pregnancy may affect neural foetal development via corticoid pathways. Using a large epidemiological cohort, this study explores the relationship between maternal somatic anxiety in pregnancy and child scores on the Test of Everyday Attention in Children (TEA-Ch).

Methods: Linear regression was used to analyse the association of maternal somatic anxiety during pregnancy and performance of children on three subtests of the TEA-Ch at age 8.5 years that assess selective attention (Sky Search), sustained attention (Sky Search Dual Test) and attentional control (Opposite Worlds).

Results: Children with complete data on each subtest were included in the analysis, comprising 4,198 children for the Sky Search subtest, 3,845 for the Sky Search Dual Test and 4,202 for the Opposite Worlds subtest. No association was found between exposure to maternal somatic anxiety and child's performance in any of the TEA-Ch subtests either before or after adjusting for confounders. The results did not change when stratifying by gender. Limitations: Selective attrition, lack of sensitivity of tests and lack of adjustment for the postnatal environment are possible limitations to this study.

Conclusions: We found no evidence of an association between exposure to maternal somatic anxiety in pregnancy and TEA-Ch scores. These results suggest that anxiety during pregnancy does not affect the development of children's attentional skills measured by TEA-Ch

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J Altern Complement Med. 2018;24:463-71.

EFFICACY OF HIPPOTHERAPY VERSUS PHARMACOTHERAPY IN ATTENTION-DEFICIT/HYPERACTIVITY DISORDER: A RANDOMIZED CLINICAL TRIAL.

Oh Y, Joung Y-S, Jang B, et al.

Objectives: Pharmacotherapy among children with attention-deficit/hyperactivity disorder (ADHD) is effective, but many patients suffer from secondary psychiatric problems even after improvement of ADHD core symptoms. Hippotherapy have been used as adjunct treatment options for physical and psychosocial rehabilitation as well as to ameliorate core symptoms. The aim of this study was to investigate the effects of Hippotherapy versus pharmacotherapy for children with ADHD.

Design: Thirty-four participants with ADHD were randomly assigned at a 1:1 ratio to either 24 sessions of a twice-weekly hippotherapy or pharmacotherapy. To assess therapeutic effects, the ADHD Rating Scale (ARS) was used pretreatment and posttreatment as the primary outcome measure. Secondary outcomes included the Child Behavior Checklist (CBCL), Self-Esteem Scale (SES), Pediatric Quality of Life Inventory (PedsQL) child and parent report version, Developmental Coordination Disorder Questionnaire (DCDQ), Clinical Global Impressions-Severity (CGI-S), and quantitative electroencephalography.

Results: Both groups showed marked improvements in ADHD symptoms, CGI-S. No significant differences between groups were detected regarding treatment outcome except thought problem subscales of CBCL. Twelve weeks of hippotherapy improved attention, impulsivity/hyperactivity, and quality of life.

Conclusion: This trial is promising, but further studies are required to evaluate the long-term clinical effectiveness of hippotherapy. The study is registered with ClinicalTrials.gov, number NCT 02482649

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Journal of Babol University of Medical Sciences. 2016;18:28-34.

EFFECTS OF NARRATIVE THERAPY AND COMPUTER-ASSISTED COGNITIVE REHABILITATION ON THE REDUCTION OF ADHD SYMPTOMS IN CHILDREN.

Emadian SO, Bahrami H, Hassanzade R, et al.

BACKGROUND AND OBJECTIVE: Attention deficit/hyperactivity disorder (ADHD) is the most common neurobehavioral condition in children, which adversely affects the psychological function of children in educational, social, and emotional areas. Use of non-pharmacological treatment methods, such as narrative therapy and computer-assisted cognitive rehabilitation, is necessary for ADHD patients due to lack of side

effects and concerns regarding medication therapy. This study aimed to evaluate the effects of narrative therapy and computer-assisted cognitive rehabilitation on the symptoms of ADHD in children. METHODS: This quasi-experimental study was conducted in Sari, Iran during June-February 2015 using the pretest-posttest approach with a control group. In total, 30 children aged 7-12 years diagnosed with ADHD were selected and divided into three groups. Children of the first group received eight sessions of narrative therapy, while the second group received 10 sessions of computer-assisted cognitive rehabilitation, and the third group received no training. Data were collected using the Raven's colored matrices, Conners' Parent Rating Scale (CPRS-48), and CogniPlus software.
FINDINGS: Mean post-test scores of ADHD symptoms were 20.1-¦5.21 and 20-¦3.55 in the narrative therapy and computer-assisted cognitive rehabilitation groups, respectively; however, no significant difference was observed between the groups in this regard. Moreover, these scores were 37.4-¦9.84 and 38.95-¦9.06 in the control group, which showed a significant difference compared to the experimental groups ($p<0.05$).
CONCLUSION: According to the results of this study, narrative therapy and computer-assisted cognitive rehabilitation could remarkably reduce ADHD symptoms in children

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J Clin Exp Neuropsychol. 2018 May;40:389-404.

CLINICAL FEATURES AND SUBJECTIVE/PHYSIOLOGICAL RESPONSES TO EMOTIONAL STIMULI IN THE PRESENCE OF EMOTION DYSREGULATION IN ATTENTION-DEFICIT HYPERACTIVITY DISORDER.

Taskiran C, Karaismailoglu S, Cak Esen HT, et al.

Introduction: Emotion dysregulation (ED) has long been recognized in clinical descriptions of attention-deficit hyperactivity disorder (ADHD), but a renewed interest in ED has advanced research on the overlap between the two entities. Autonomic reactivity (AR) is a neurobiological correlate of emotion regulation; however, the association between ADHD and AR remains unclear. Our aim was to explore the clinical differences, AR, and subjective emotional responses to visual emotional stimuli in ADHD children with and without ED.
Method: School-aged ADHD children with (n = 28) and without (n = 20) ED, according to the definition of deficiency in emotional self-regulation (DESR), and healthy controls (n = 22) were interviewed by using the Schedule for Affective Disorders and Schizophrenia for School Aged Children–Present and Lifetime version (K-SADS-PL) to screen frequent psychopathologies for these ages. All subjects were evaluated with Child Behavior Checklist 6–18 (CBCL), the Strengths and Difficulties Questionnaire (SDQ), the McMaster Family Assessment Device (FAD), the School-Age Temperament Inventory (SATI), and Conners' Parent Rating Scale (CPRS-48), which were completed by parents. To evaluate emotional responses, the International Affective Picture System (IAPS) and the subjective and physiological responses (electrodermal activity and heart rate reactivity) to selected pictures were examined.
Results: Regarding clinically distinctive features, the ADHD+ED group differed from the ADHD–ED and the control groups in terms of having higher temperamental negative reactivity, more oppositional/conduct problems, and lower prosocial behaviors. In the AR measures, children in the ADHD+ED group rated unpleasant stimuli as more negative, but they still had lower heart rate reactivity (HRR) than the ADHD–ED and control groups; moreover, unlike the two other groups, the ADHD+ED group showed no differences in HRR between different emotional stimuli.
Conclusion: The presented findings are unique in terms of their ability to clinically and physiologically differentiate between ADHD children with and without ED

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J Clin Psychiatry. 2018;79.

THE MIXED OPIOID RECEPTOR ANTAGONIST NALTREXONE MITIGATES STIMULANT-INDUCED EUPHORIA: A DOUBLE-BLIND, PLACEBO-CONTROLLED TRIAL OF NALTREXONE.

Spencer TJ, Bhide P, Zhu J, et al.

Objective: Supratherapeutic doses of methylphenidate activate ++-opioid receptors, which are linked to euphoria. This study assessed whether naltrexone, a mixed ++-opioid antagonist, may attenuate the euphoric

effects of stimulants, thereby minimizing their abuse potential in subjects with attention-deficit/hyperactivity disorder (ADHD).
Methods: We conducted a 6-week, double-blind, placebo-controlled, randomized clinical trial of naltrexone in adults with DSM-IV ADHD receiving open treatment with a long-acting formulation of methylphenidate (January 2013 to June 2015). Spheroidal Oral Drug Absorption System methylphenidate (SODAS-MPH) was administered twice daily, was titrated to Γê+1 mg/kg/d over 3 weeks, and was continued for 3 additional weeks depending on response and adverse effects. Subjects were adults with ADHD preselected for having experienced euphoria with an oral test dose of 60 mg of immediate-release methylphenidate (IR-MPH). The primary outcome measure was Question 2 (Liking a Drug Effect) on the Drug Rating Questionnaire, Subject version, which was assessed after oral test doses of 60 mg of IR-MPH were administered after the third and sixth weeks of treatment with SODAS-MPH.
Results: Thirty-seven subjects who experienced stimulant-induced (mild) euphoria at a baseline visit were started in the open trial of SODAS-MPH and randomized to naltrexone 50 mg/d or placebo. Thirty-one subjects completed through week 3, and 25 completed through week 6. Naltrexone significantly diminished the euphoric effect of IR-MPH during the heightened-risk titration phase (primary outcome; first 3 weeks) (2 = 5.07, P =.02) but not the maintenance phase (weeks 4-6) (2 = 0.22, P =.64) of SODAS-MPH treatment.
Conclusions: Preclinical findings are extended to humans showing that naltrexone may mitigate stimulant-associated euphoria. Our findings provide support for further studies combining opioid receptor antagonists with stimulants to reduce abuse potential

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J Clin Psychiatry. 2018;79.

SLUGGISH COGNITIVE TEMPO AS A POSSIBLE PREDICTOR OF METHYLPHENIDATE RESPONSE IN CHILDREN WITH ADHD: A RANDOMIZED CONTROLLED TRIAL.

Froehlich TE, Becker SP, Nick TG, et al.

Objective: To examine whether sluggish cognitive tempo (SCT) symptomatology moderates dose response to methylphenidate and whether the impact of SCT on medication response is distinct from attention-deficit/hyperactivity disorder (ADHD) subtype effects.
Methods: Stimulant-naive children with ADHD predominantly inattentive type (ADHD-I; n = 126) or ADHD combined type (ADHD-C; n = 45) aged 7-11 years were recruited from the community from September 2006 to June 2013 to participate in a prospective, randomized, double-blind, 4-week crossover trial of long-acting methylphenidate. ADHD diagnosis and subtype were established according to DSM-IV criteria using a structured interview and teacher ADHD symptom ratings. SCT symptoms were assessed using a teacher-rated scale with 2 factors (Sluggish/Sleepy and Daydreamy). Primary outcomes included (1) categorization of children as methylphenidate responders, methylphenidate nonresponders, or placebo responders by 2 blinded physicians and (2) parent and teacher ratings of child behavior on the Vanderbilt ADHD Diagnostic Rating Scales while subjects were on treatment with placebo or 1 of 3 methylphenidate dosages (low, medium, high).
Results: Increased SCT Sluggish/Sleepy factor scores were associated with being a methylphenidate nonresponder or placebo responder rather than a methylphenidate responder (P =.04). Sluggish/Sleepy factor scores were also linked to diminished methylphenidate dose response for parent-and teacher-rated inattention symptoms (Sluggish/Sleepy factor dose P =.004). SCT Daydreamy symptoms and ADHD subtype (ADHD-I vs ADHD-C) were not associated with methylphenidate responder status and did not moderate methylphenidate dose response for inattention symptoms.
Conclusions: SCT Sluggish/Sleepy symptoms, but not SCT Daydreamy symptoms or ADHD subtype, predicted methylphenidate nonresponse. This novel finding, if replicated, may have important implications for assessing SCT as part of ADHD care

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J Clin Psychopharmacol. 2018;38:254-59.

MATERNAL ANTIDEPRESSANT USE DURING PREGNANCY AND THE RISK OF ATTENTION-DEFICIT/HYPERACTIVITY DISORDER IN CHILDREN: A SYSTEMATIC REVIEW OF THE CURRENT LITERATURE.

Uguz F.

Purpose This study reviewed the current literature examining the potential relationship between use of antidepressants during pregnancy and attention-deficit/hyperactivity disorder (ADHD) in children.

Methods PubMed was searched for English language reports between January 1, 1995, and July 31, 2017, by using combinations of the key words pregnancy, antidepressants, selective serotonin reuptake inhibitors (SSRIs), selective serotonin-norepinephrine reuptake inhibitors (SNRIs), tricyclic antidepressants (TCAs), children, offspring, and ADHD. Studies that reported association between ADHD in children and use of antidepressant in pregnant women were included in the review.

Results A total of 7 relevant studies that met the review criteria were examined. The studies reported that compared with nonusers adjusted risks of ADHD in children were 1.2 to 1.6 for the use of any antidepressant, 0.91 to 1.66 for selective serotonin reuptake inhibitors, 1.1 to 1.4 for selective serotonin-norepinephrine reuptake inhibitors, and 1.1 to 1.8 for tricyclic antidepressants. There was some scientific evidences suggesting a connection between antidepressant use during all trimesters of pregnancy and increased risk of ADHD in children. In addition, the study results suggest that underlying maternal anxiety or depressive disorders may also contribute to increased risk of ADHD.

Implications Although some studies have suggested a moderately increased risk of ADHD in children with maternal antidepressant use during pregnancy, based on limitations and results of the studies, this review concluded that there is no strong evidence to suggest a causal link

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J Health Econ. 2018;60:1-15.

EXPLODING ASTHMA AND ADHD CASELOADS: THE ROLE OF MEDICAID MANAGED CARE.

Chorniy A, Currie J, Sonchak L.

In the U.S., nearly 11% of school-age children have been diagnosed with ADHD, and approximately 10% of children suffer from asthma. In the last decade, the number of children diagnosed with these conditions has inexplicably been on the rise. This increase has been concentrated in the Medicaid caseload nationwide. One of the most striking changes in Medicaid has been the transition from fee-for-service (FFS) reimbursement to Medicaid managed care (MMC), which had taken place in 80% of states by 2016. Using Medicaid claims from South Carolina, we show that this change contributed to the increase in asthma and ADHD caseloads. Empirically, we rely on variation in MMC enrollment due to a change in the ΓÇ£defaultΓÇØ Medicaid plan from FFS to MMC, and on rich panel data that allow us to follow the same children before and after they were required to switch. We find that the transition from FFS to MMC explains about a third of the rise in the number of Medicaid children being treated for ADHD and asthma, along with increases in treatment for many other conditions. These are likely to be due to the incentives created by the risk adjustment and quality control systems in MMC

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J Isfahan Med Sch. 2006;24:61-67.

COMPARATIVE OF EXECUTIVE FUNCTION IN TOURETT'S SYNDROME IN CHILDREN WITH AND WITHOUT ADHD.

Karahmadi M, Shahrivar Z.

Introduction Evaluation of Executive Function in children and adolescent's with Tourett's syndrome with and without Attention deficit Hyperactive Disorder.

Method A descriptive- analytic (case-control) study. They study was per Formed in children and adolescents psychiatric clinic of Rozbeh hospital during 1381-1383 By means of clinical psychiatric evalution k-sads and DSM-IV criteria 26-child and adolescent (7-17 year) who were diagnosed as having ADHD with tourett and tourett were entrolled in study. Also 15 healthy Matched subjects were entrolled as a control group. In each group Tower of London- Yale-conners was used.

Results and Discussion In comparsion of 3 group, children and adolesent's with Tourett's & ADHD in attention, planning, working memory Impulsivity (Executive Function) had impaired

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Journal of Neural Engineering. 2018;15.

IDENTIFYING ADHD CHILDREN USING HEMODYNAMIC RESPONSES DURING A WORKING MEMORY TASK MEASURED BY FUNCTIONAL NEAR-INFRARED SPECTROSCOPY.

Gu Y, Miao S, Han J, et al.

Objective. Attention-deficit/hyperactivity disorder (ADHD) is a neurodevelopmental disorder affecting children and adults. Previous studies found that functional near-infrared spectroscopy (fNIRS) can reveal significant group differences in several brain regions between ADHD children and healthy controls during working memory tasks. This study aimed to use fNIRS activation patterns to identify ADHD children from healthy controls.

Approach. FNIRS signals from 25 ADHD children and 25 healthy controls performing the n-back task were recorded; then, multivariate pattern analysis was used to discriminate ADHD individuals from healthy controls, and classification performance was evaluated for significance by the permutation test.

Main results. The results showed that 86.0% () of participants can be correctly classified in leave-one-out cross-validation. The most discriminative brain regions included the bilateral dorsolateral prefrontal cortex, inferior medial prefrontal cortex, right posterior prefrontal cortex, and right temporal cortex.

Significance. This study demonstrated that, in a small sample, multivariate pattern analysis can effectively identify ADHD children from healthy controls based on fNIRS signals, which argues for the potential utility of fNIRS in future assessments

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J Paediatr Child Health. 2018;54:20.

HIGH DOSE STIMULANT MEDICATION FOR THE MANAGEMENT OF ATTENTION DEFICIT/HYPERACTIVITY DISORDER (ADHD): A RETROSPECTIVE COHORT STUDY.

Ross L, Sapre V, Stanislaus C, et al.

Introduction: The maximum doses of stimulants used for treating ADHD are based on convention rather than scientific data.1 The NSW prescribing criteria define high dose (HD) as: methylphenidate >2mg/kg or >108mg/day; dexamphetamine >1mg/kg or >50mg/kg/day; lisdexamfetamine >70mg/day2. HD can be prescribed on application to the NSW Ministry of Health (MoH), given supporting documentation of efficacy from an independent observer. In the studied practice the treatment dose was prescribed on clinical grounds. The aim of this study is to describe the clinical characteristics of children authorised by the NSW MoH to receive HD stimulants and compare them to those on regular doses (RD).

Methods: Clinical records of children treated with HD stimulant were compared with those of controls prescribed RD. Controls had a prescription on the same day that a study child commenced HD, identified using a database of prescription records. The data spanned 2003-2016, including children from a public hospital clinic and private consulting rooms. Categorical data were compared using chi-square and continuous data using independent samples t-tests. Growth data were analysed in age and sex specific z-scores.

Results: There were 51 HD and 119 RD children. The HD children were more likely than RD children to have oppositional defiant disorder (ODD)(82% vs 55%, p=0.001), and started medication at a younger age (6.4-1.7 years vs 8.3-2.8 years, p<0.001). Of the HD children, 46 had trialled HD methylphenidate: maximum dose 82.1-33.1mg/day, 2.3-0.4mg/kg/day. All had documented evidence of improvement on HD from an independent observer. HD children were more likely to take risperidone (37% vs 16%, p=0.002) but not other psychotropic drugs. Dose reductions were necessitated in 33% (n=17) HD and 27% of RD children (p=0.2); the commonest reason in HD children was worsening behaviour (n=7). The HD children grew significantly slower in height and weight (change in height z-score -0.43-0.55 vs -0.09-0.58, p<0.001, change in weight z-score -0.56-0.81 vs -0.19-0.67, p=0.002) over a treatment period of 5.1-3.0 and 4.2-3.2 years respectively. No child had a dose reduction due to hypertension.

Conclusions: Compared with RD, children on HD stimulant showed evidence of greater impairment. They started treatment at a younger age and had a higher prevalence of ODD. Over an average treatment period of >4 years, they showed a greater decline in z-scores for height and weight. Dose reductions due to side effects happened no more frequently than in children on standard doses

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J Pediatr Psychol. 2018 Mar;43:162-71.

CHILDHOOD ADHD SYMPTOMS AND FUTURE ILLICIT DRUG USE: THE ROLE OF ADOLESCENT CIGARETTE USE.

Lee CT, McClernon FJ, Kollins SH, et al.

Objectives: The aim of this study is to understand how early cigarette use might predict subsequent illicit drug use, especially among individuals with attention-deficit hyperactivity disorder (ADHD) symptoms during childhood.

Methods: Data were drawn from the National Longitudinal Study of Adolescent Health (Waves I–IV). The analysis sample involves participants who had not used illicit drugs at Wave I, with no missing responses for studied predictors (N = 7,332).

Results: Smoking status at Wave I (ever regular vs. never regular) and childhood ADHD symptoms predicted subsequent illicit drug use at Waves II to IV. No interaction effect of smoking status at Wave I and childhood ADHD symptoms was found. However, an indirect effect from childhood ADHD symptoms on illicit drug use was identified, through smoking status at Wave I. Similar results were observed for predicting illicit drug dependence.

Conclusions: The findings support the notion that smoking status during early adolescence may mediate the association between childhood ADHD symptoms and risk of later adult drug use. Interventions to prevent smoking among adolescents may be particularly effective at decreasing subsequent drug use, especially among children with ADHD symptoms

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J Pediatr. 2018.

A PROSPECTIVE BIRTH COHORT STUDY ON EARLY CHILDHOOD LEAD LEVELS AND ATTENTION DEFICIT HYPERACTIVITY DISORDER: NEW INSIGHT ON SEX DIFFERENCES.

Ji Y, Hong X, Wang G, et al.

Objective: To investigate the prospective associations between early childhood lead exposure and subsequent risk of attention deficit hyperactivity disorder (ADHD) in childhood and its potential effect modifiers.

Study design: We analyzed data from 1479 mother-infant pairs (299 ADHD, 1180 neurotypical) in the Boston Birth Cohort. The child's first blood lead measurement and physician-diagnosed ADHD was obtained from electronic medical records. Graphic plots and multiple logistic regression were used to examine dose-response associations between lead exposure and ADHD and potential effect modifiers, adjusting for pertinent covariables.

Results: We found that 8.9% of the children in the Boston Birth Cohort had elevated lead levels (5-10 -Ág/dL) in early childhood, which was associated with a 66% increased risk of ADHD (OR, 1.66; 95% CI, 1.08-2.56). Among boys, the association was significantly stronger (OR, 2.49; 95% CI, 1.46-4.26); in girls, the association was largely attenuated (P value for sex-lead interaction =.017). The OR of ADHD associated with elevated lead levels among boys was reduced by one-half if mothers had adequate high-density lipoprotein levels compared with low high-density lipoprotein, or if mothers had low stress compared with high stress during pregnancy.

Conclusions: Elevated early childhood blood lead levels increased the risk of ADHD. Boys were more vulnerable than girls at a given lead level. This risk of ADHD in boys was reduced by one-half if the mother had adequate high-density lipoprotein levels or low stress. These findings shed new light on the sex difference in ADHD and point to opportunities for early risk assessment and primary prevention of ADHD

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J Psychiatry Neurosci. 2018;43:151-60.

ALTERED CORTICAL THICKNESS AND ATTENTIONAL DEFICITS IN ADOLESCENT GIRLS AND WOMEN WITH BULIMIA NERVOSA.

Berner LA, Stefan M, Lee S, et al.

Background: Frontostriatal and frontoparietal abnormalities likely contribute to deficits in control and attentional processes in individuals with bulimia nervosa and to the persistence of dysregulated eating across development. This study assessed these processes and cortical thickness in a large sample of adolescent girls and women with bulimia nervosa compared with healthy controls.

Methods: We collected anatomical MRI data from adolescent girls and women (ages 12-38 yr) with full or subthreshold bulimia nervosa and age-matched healthy controls who also completed the Conners Continuous Performance Test-II (CPT-II). Groups were compared on task performance and cortical thickness. Mediation analyses explored associations among cortical thickness, CPT-II variables, bulimia nervosa symptoms and age.

Results: We included 60 girls and women with bulimia nervosa and 54 controls in the analyses. Compared with healthy participants, those with bulimia nervosa showed increased impulsivity and inattention on the CPT-II, along with reduced thickness of the right pars triangularis, right superior parietal and left dorsal posterior cingulate cortices. In the bulimia nervosa group, exploratory analyses revealed that binge eating frequency correlated inversely with cortical thickness of frontoparietal and insular regions and that reduced frontoparietal thickness mediated the association between age and increased symptom severity and inattention. Binge eating frequency also mediated the association between age and lower prefrontal cortical thickness.

Limitations: These findings are applicable to only girls and women with bulimia nervosa, and our cross-sectional design precludes understanding of whether cortical thickness alterations precede or result from bulimia nervosa symptoms.

Conclusion: Structural abnormalities in the frontoparietal and posterior cingulate regions comprising circuits that support control and attentional processes should be investigated as potential contributors to the maintenance of bulimia nervosa and useful targets for novel interventions

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J Psychopathol Behav Assess. 2018;1-12.

SOCIAL PROBLEMS IN ADHD: IS IT A SKILLS ACQUISITION OR PERFORMANCE PROBLEM?

Aduen PA, Day TN, Kofler MJ, et al.

Recent models suggest that social skills training's inefficacy for children with ADHD may be due to target misspecification, such that their social problems reflect inconsistent performance rather than knowledge/skill gaps. No study to date, however, has disentangled social skills acquisition from performance deficits in children with ADHD. Children ages 8-12 with ADHD (n = 47) and without ADHD (n = 23) were assessed using the well-validated social behavioral analysis framework to quantify cross-informant social skills acquisition deficits, performance deficits, and strengths. Results provided support for the construct and predictive validities of this Social Skills Improvement System (SSIS) alternate scoring method, including expected magnitude and valence relations with BASC-2 social skills and ADHD symptoms based on both parent and teacher report. Acquisition deficits were relatively rare and idiosyncratic for both the ADHD and Non-ADHD groups, whereas children with ADHD demonstrated cross-informant social performance deficits (d = 0.82-0.99) on several specific behaviors involving attention to peer directives, emotion regulation, and social reciprocity. Relative to themselves, children with ADHD were perceived by parents and teachers as exhibiting more social strengths than social acquisition deficits; however, they demonstrated significantly fewer social strengths than the Non-ADHD group (d = 0.71 to 0.89). These findings are consistent with recent conceptualizations suggesting that social problems in ADHD primarily reflect inconsistent performance rather than a lack of social knowledge/skills. Implications for refining social skills interventions for ADHD are discussed

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Journal of Psychosomatic Obstetrics and Gynecology. 2018;1-9.

MATERNAL PSYCHOSOCIAL STRESS AND CHILDREN'S ADHD DIAGNOSIS: A PROSPECTIVE BIRTH COHORT STUDY.

Okano L, Ji Y, Riley AW, et al.

Objective: Examine the association of mothers' psychosocial stressors before and during pregnancy with their childrenΓÇÖs diagnosis of attention deficit hyperactivity disorder (ADHD).

Methods: This study included 2140 motherΓÇôchild pairs who had at least one postnatal pediatric visit at the Boston Medical Center between 2003 and 2015. Child ADHD was determined via International Classification of Diseases, Ninth Revision (ICD-9) codes documented in electronic medical records. Latent factors of maternal stress and social support and measures of the physical home environment and psychosocial adversities were constructed using exploratory factor analysis. The association between the latent factors and child ADHD diagnosis was examined using multiple logistic regression, controlling for known risk factors for ADHD.

Results: Children were 1.45 (95% CI: 1.06, 1.99) and 3.03 (95% CI: 2.19, 4.20) times more likely to receive an ADHD diagnosis if their mother experienced a major stressful event during pregnancy or reported a high level of perceived stress, respectively. The number of family adversities increases the risk of ADHD diagnosis [second quartile: OR = 1.90; CI (1.31, 2.77); third quartile: OR = 1.96 CI (1.34, 2.88); fourth quartile: OR = 2.89 CI (2.01, 4.16)] compared to first quartile.

Conclusions: In this prospective, predominantly urban, low-income, minority birth cohort, mothers' psychosocial stress before and during pregnancy appears to be an independent risk factor for the development of ADHD in their children

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J Am Acad Child Adolesc Psychiatry. 2018 Apr;57:245-51.

SUSTAINED EFFECTS OF COLLABORATIVE SCHOOL-HOME INTERVENTION FOR ATTENTION-DEFICIT/HYPERACTIVITY DISORDER SYMPTOMS AND IMPAIRMENT.

Pfiffner LJ, Rooney ME, Jiang Y, et al.

Objectives: The Collaborative Life Skills (CLS) program is a school-home intervention for students with attention-deficit/hyperactivity disorder (ADHD) symptoms and impairment. CLS integrates school, parent, and student treatments followed by booster sessions during a maintenance period into the subsequent school year. The program is delivered by school-based mental health providers. Beneficial post-treatment effects have been documented. This study evaluated the effects of CLS after the maintenance period in the subsequent school year.

Method: Using a cluster randomized design, schools within a large urban public school district were randomly assigned to CLS (12 schools) or usual services (11 schools). Approximately 6 students participated at each school (N = 135, grade range = 2–5). Measures were completed at baseline, after treatment, and follow-up during the next school year.

Results: Students from schools assigned to CLS compared with those assigned to usual services showed significantly greater improvement at follow-up on parent, but not teacher, ratings of ADHD and oppositional defiant disorder symptom severity, organizational skills, and global impairment. Within-group analyses indicated that parent- and teacher-reported post-treatment gains for CLS in ADHD and oppositional defiant disorder symptoms, organizational skills, and academic competence were maintained into the next school year.

Conclusions: These results extend support for CLS to the following school year by demonstrating sustained benefits on parent-reported ADHD and oppositional defiant disorder symptoms and functional impairment. The lack of significant teacher-reported differences between CLS and usual services highlights the need for further study of booster treatments for improving outcomes with new teachers across school years

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J Am Acad Child Adolesc Psychiatry. 2018;57:343-50.

HAS THE PREVALENCE OF CHILD AND ADOLESCENT MENTAL DISORDERS IN AUSTRALIA CHANGED BETWEEN 1998 AND 2013 TO 2014?

Sawyer MG, Reece CE, Sawyer ACP, et al.

Objective: This study examined whether the 12-month prevalence of major depressive disorder (MDD), attention-deficit/hyperactivity disorder (ADHD), and conduct disorder (CD) among 6- to 17-year-olds in Australia changed between 1998 and 2013 to 2014. It also investigated whether changes in the prevalence of disorders over this time varied for children living in families containing 2 parents versus single parents, and families with high versus low income.

Method: The study used data from national surveys conducted in Australia in 1998 (N = 3,597) and 2013 to 2014 (N = 5,359). In both surveys, the participating individuals were randomly selected from all 6- to 17-year-olds in Australia, and mental disorders were assessed using the Diagnostic Interview Schedule for Children Version IV (DISC-IV), completed by parents.

Results: There was little change in the overall prevalence of mental disorders between 1998 (12.5%, 95% CI = 11.4-13.7) and 2013 to 2014 (11.1%, 95% CI = 10.1-12.2). Although there were some differences in the changes for children with different disorders, most were small in magnitude. Specifically, MDD prevalence increased from 2.1% (95% CI = 1.7-2.7) to 3.2% (95% CI = 2.7-3.8), ADHD prevalence declined from 9.9% (95% CI = 8.9-10.9) to 7.8% (95% CI = 6.9-8.7), and CD prevalence declined from 2.7% (95% CI = 2.2-3.3) to 2.1% (95% CI = 1.7-2.7). There was a persisting pattern of higher prevalence among children living in single-parent and low-income households.

Conclusion: Lack of change at a population level in the prevalence of child mental disorders suggests that new innovations in research, policy, and practice are needed to successfully address the major public health problem posed by child and adolescent mental disorders in the community

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J Can Acad Child Adolesc Psychiatry. 2018;27:148-51.

STIMULANT WITHDRAWAL IN A CHILD WITH AUTISM SPECTRUM DISORDER AND ADHD - A CASE REPORT.

Krakowski A, Ickowicz A.

Objective: To consider whether the concepts of tolerance and withdrawal to stimulant medications apply to a pre-adolescent female, affected by autism spectrum disorder (ASD) and treated for associated attention-deficit/hyperactivity disorder (ADHD).

Methods: We describe the case history and review scientific English language literature pertaining to acute withdrawal effects associated with methylphenidate and amphetamine derivatives in children.

Results: An 11-year-old female with ASD and ADHD referred to our clinic experienced vomiting, headaches, and light sensitivity following abrupt discontinuation of methylphenidate; she subsequently presented with migraines and marked malaise immediately after a dose reduction in lisdexamfetamine. Evidence supports the notion that ADHD symptoms in children with ASD can be effectively treated with methylphenidate; however, beneficial effects are less robust relative to children with a primary ADHD diagnosis. Children affected by ASD are also more susceptible to adverse effects. Literature on withdrawal from stimulants in children is limited to case studies; in contrast, in the adult population more information is available, especially in adults with substance abuse disorders. Adults experiencing stimulant withdrawal often experience depression, fatigue, changes in appetite, and insomnia or hypersomnia.

Conclusions: We argue that tolerance to stimulants was conceivably developing in this young female, and consequently discontinuation of methylphenidate and dose reduction of lisdexamfetamine resulted in withdrawal symptoms. Children with ASD are more sensitive to stimulant medications and we wonder whether this extends to an increased sensitivity to developing tolerance to stimulant medication. Clinicians ought to be vigilant about the emergence of symptomology suggestive of withdrawal phenomena following stimulant discontinuation

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Medical Journal of Indonesia. 2018;27:44-53.

COMPLIANCE IN DOING SENAM KESEGARAN JASMANI 1988 EXERCISE IMPROVES CARDIORESPIRATORY ENDURANCE OF ATTENTION DEFICIT/HYPERACTIVITY DISORDER CHILDREN.

Mirtha LT, Sekartini R.

Background: Physical exercise was hypothesized to be able to improve the behavior of children with attention deficit/ hyperactivity disorder (ADHD) by improving attention and concentration. Several studies mentioned that physical exercise could make ADHD children calmer, not only as a supportive therapy, but also as a therapeutic therapy. The aim of this study was to evaluate the effects of physical exercise to the behavior of ADHD patients and to analyze the effects of Senam Kesegaran Jasmani 1988 (SKJ 88) exercise compliance to the cardiorespiratory endurance in ADHD children.
Methods: This study was an experimental study with 40 subjects from a special needs school in Tangerang, Indonesia. Subjects were given SKJ 88 exercise for 8 weeks, and the level of cardiorespiratory endurance was assessed with 600 m run before and after intervention.
Results: 21 subjects (52.5%) were compliant, and the rest were very compliant. Although statistical analysis showed that there was no significant difference in cardiorespiratory endurance before and after intervention, the mean results of cardiorespiratory endurance test before intervention was higher than after. Mean time spent in the 600-m run before intervention was 497.9 seconds (SD 73.53), and after intervention was 313.7 seconds (SD 43.28).
Conclusion: Based on the statistical test, we concluded that there was significant decrease of time spent for cardiorespiratory endurance test ($p<0.001$). The reduction of time taken to run 600 m by 184.3 seconds (SD 73.33) showed the improvement of cardiorespiratory endurance after the treatment

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Neuro Endocrinol Lett. 2017 Dec;38:389-96.

THE IMPACT OF AIR POLLUTION TO CENTRAL NERVOUS SYSTEM IN CHILDREN AND ADULTS.

Sram RJ, Veleminsky M, Jr., Veleminsky M, Sr., et al.

The aim of this paper was to review studies analyzing the associations between air pollution and neurodevelopment in children as well as the effect on adult population. Effect of prenatal exposure to polycyclic aromatic hydrocarbons (PAHs, benzo[a]pyrene, B[a]P) were already studied on cohorts from New York, Poland, China, and Spain. All results indicate changes of child behavior and neurodevelopment at the age of 3-9 years, decrease of IQ, increase of Attention Deficit Hyperactivity Disorder (ADHD), decrease of brain-derived neurotrophic factor (BDNF), reduction of left hemisphere white matter. Effect of traffic-related air pollution (TRAP) to neurobehavioral development in children, measured as PM2.5 (particulate matter <2.5 microm), PM10, elemental carbon (EC), black smoke (BC), NO2, NOx, were studied in USA, Spain, Italy, and South Korea. Increased concentrations of TRAP were associated with the increase of ADHD, autism, affected cognitive development; PM2.5 decreased the expression of BDNF in placenta. Increased concentrations of PM2.5 affected adults cognition (episodic memory), increased major depressive disorders. Increased concentrations of NO2 were associated with dementia, NOx with Parkinson's disease. Increased concentrations of PAHs, PM2.5 and NO2 in polluted air significantly affect central nervous system in children and adults and represent a significant risk factor for human health

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

QTC PROLONGATION AFTER ADHD MEDICATION.

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

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

METHODS: We included 69 patients from a region of central Slovakia, 36 patients were taking atomoxetine and 33 patients methylphenidate. QTc, heart rate, potassium levels and BMI were examined before and after 8 weeks of treatment. Therapeutic effect was measured by ADHD-RS-IV.
RESULTS: We found QTc prolongation after 8 weeks of treatment both with atomoxetine and methylphenidate that was neither followed by the significant changes in BMI and potassium levels nor the significant increase of heart rate.
CONCLUSION: This is the first study revealing QTc prolongation in the group of ADHD children from the same region after 8-week treatment with atomoxetine and methylphenidate, indicating the potential discrete abnormalities in cardiac functioning associated with polymorphisms in genes of dopaminergic and noradrenergic system

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NeuroImage Clin. 2018;19:527-37.
EFFECTS OF MULTISENSORY STIMULI ON INHIBITORY CONTROL IN ADOLESCENT ADHD: IT IS THE CONTENT OF INFORMATION THAT MATTERS.
Chmielewski WX, Tiedt A, Bluschke A, et al.
Even though deficits in inhibitory control and conflict monitoring are well-known in ADHD, factors that further modulate these functions remain to be elucidated. One factor that may be of considerable importance is how inhibitory control is modulated by multisensory information processing. We examined the influence of concurrent auditory conflicting or redundant information on visually triggered response inhibition processes in adolescent ADHD patients and healthy controls. We combined high-density event-related potential (ERP) recordings with source localization to delineate the functional neuroanatomical basis of the involved neurophysiological processes. In comparison to controls, response inhibition (RI) processes in ADHD were compromised in conflicting conditions, but showed no differences to controls when redundant or no concurrent auditory information was presented. These effects were reflected by modulations at the response selection stage (P3 ERP) in the medial frontal gyrus (BA32), but not at the attentional selection (P1, N1 ERPs) or resource allocation level (P2 ERP). Conflicting information during RI exerts its influences in adolescent ADHD via response selection mechanisms, but not via attentional selection. It is not the mere presence of concurrent information, but the presence of conflicting information during RI that may destabilize goal shielding processes in medial frontal cortical regions, by means of increasing the automaticity of response tendencies. The occurring RI deficits might relate to the increased impulsivity in adolescent ADHD and a corresponding vulnerability to react to an increased automaticity of pre-potent response tendencies. ADHD patients show a bias to a specific content of information which can modulate inhibitory control

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Neurology. 2018;90.
IRON AND FERRITIN LEVELS IN PATIENTS WITH ADHD.
Agarwal S, Gupta S, Pecor K, et al.
Objective: To study the levels of iron and ferritin in children with attention deficit hyperactivity disorder (ADHD). Background: ADHD is a complex neurologic disorder, the pathogenesis of which remains unclear. Iron is a implicated in brain dopaminergic activity. Recent studies have shown an association with low iron, as well as ferritin, levels with ADHD but the results are inconsistent. Furthermore, association with anemia has been unclear.
Design/Methods: Iron, ferritin, hematocrit and hemoglobin data were collected from 71 individuals representing hyperactive (N = 12), inattentive (N = 17), and combined (N = 42) forms of ADHD. Control data were in the form of clinical reference values (mean and standard deviation) from the laboratory. Due to lack of sample sizes for the control data, one-way ANOVA for each of the above variables that included the control group and the three ADHD groups could not be performed. Instead, data were first contrasted among ADHD types for each value using oneway ANOVA. There were no differences for any variable, so the data were pooled among ADHD types and tested for deviation from the reference mean for each variable using one-sample t-tests.

Results: Mean age (range) of the sample was 9.4 (4-19) years. The following were the mean values of iron, ferritin, hematocrit and hemoglobin in children with ADHD (versus control values): Iron 81 (108.5) mcg/dL, ferritin 45.5 (215) ng/ml, hematocrit 38.33 (40)%, hemoglobin 12.73 (13.5) g/dL. In children with ADHD, levels of iron ($p<0.001$), ferritin ($p<0.001$), hematocrit ($p=0.001$), and hemoglobin ($p<0.001$) were significantly lower than reference ranges.
Conclusions: Serum levels of iron, ferritin were significantly lower in children with ADHD, who also had significantly lower hemoglobin and hematocrit. The ADHD subtype did not significantly influence these abnormalities

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Neurosci Behav Physiol. 2018;48:383-87.
IMPULSIVITY IN ADOLESCENTS WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER.
Chutko LS, Surushkina SY, Yakovenko EA, et al.
Objectives. To study impulsivity in adolescents with attention deficit hyperactivity disorder (ADHD) and to evaluate the efficacy of Noofen (500 mg/day for 45 days) in the treatment of this pathology.
Materials and methods. The results of clinical, psychological, and psychophysiological studies of 60 adolescents aged 12-15 years with ADHD are presented. The clinical pictures of illness and data from psychophysiological studies in ADHD with a predominance of hyperactivity (ADHD-H) and the combined type of illness (ADHD-C) were compared.
Results and conclusions. Significantly higher levels of impulsivity and anxiety were found in children with ADHD-H. Treatment with Noofen was shown to have high clinical efficacy: status improved in 63.3% of patients

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Nord J Psychiatry. 2018;1-6.
ASSOCIATION BETWEEN ALTERED LIPID PROFILES AND ATTENTION DEFICIT HYPERACTIVITY DISORDER IN BOYS.
Avcil S.
Background: Attention-deficit/hyperactivity disorder (ADHD) is a neurodevelopmental disorder, which is multifactorial, complex, and seen most commonly in childhood. Aims: The aim of this study was to examine the hypothesis that altered serum lipid profiles are associated with ADHD.
Methods: The study inluded 32 boys diagnosed with ADHD according to DSM-IV-R criteria and a control group of 29 healthy subjects. All patients were assessed with The Kiddie Schedule for Affective Disorders and Schizophrenia Present and Lifetime Version, the Turgay DSM-IV-based Disruptive Behavior Disorders Child and Adolescent Rating and Screening Scale, the Conners Parent Rating Scale-Revised Long Form, and the Conners Teacher Rating Scale. Measurements were taken of fasting plasma total cholesterol (T-Chol), triglyceride (TG), high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), and 1-day food intake levels, and the groups were compared.
Results: The mean TC, LDL, and HDL levels were significantly lower in the ADHD group than the control group ($p = .005$, $p < .001$, $p = .002$, respectively). There was no significant difference between the groups' TG levels ($p = .295$). No significant differences were determined between the combined-type ADHD patients and the predominantly inattentive subtype of ADHD in respect to the lipid profile.
Conclusion: The results of this study add to the growing body of evidence indicating an association between serum cholesterol and ADHD in boys. Further genetic and molecular studies are required to elucidate the biochemical mechanisms underlying this relationship

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Pediatr Neurol. 2018;81:25-30.

ANTECEDENTS OF SCREENING POSITIVE FOR ATTENTION DEFICIT HYPERACTIVITY DISORDER IN TEN-YEAR-OLD CHILDREN BORN EXTREMELY PRETERM.

Leviton A, Hooper SR, Hunter SJ, et al.

Background: The incidence of attention deficit hyperactivity disorder is higher among children born very preterm than among children who are mature at birth.

Methods: We studied 583 ten-year-old children who were born before 28 weeks of gestation whose IQ was above 84 and had a parent-completed Child Symptom Inventory-4, which allowed classification of the child as having or not having symptoms of attention deficit hyperactivity disorder. For 422 children, we also had a teacher report, and for 583 children, we also had a parent report of whether or not a physician made an attention deficit hyperactivity disorder diagnosis.

Results: The risk profile of screening positive for attention deficit hyperactivity disorder based on a parent's report differed from the risk profile based on the teacher's report, whereas the risk profile according to a physician and according to any two observers closely resembled the parent-reported profile. Among the statistically significant risk factors were young maternal age (parent, physician, and two observers), maternal obesity (parent, physician, and two observers), maternal smoking (parent, physician, and two observers), magnesium given at delivery for seizure prophylaxis (parent and two observers), recovery of Mycoplasma sp. from the placenta (teacher and two observers), low gestational age (parent and two observers), low birth weight (teacher and physician), singleton (parent, physician, and two observers), male (parent, teacher, physician, and two observers), mechanical ventilation on postnatal day seven (physician), receipt of a sedative (parent and two observers), retinopathy of prematurity (parent), necrotizing enterocolitis (physician), antibiotic receipt (physician and two observers), and ventriculomegaly on brain scan (parent and two observers).

Conclusions: The multiplicity of risk factors identified can be subsumed as components of four broad themes: low socioeconomic state, immaturity or vulnerability, inflammation, and epigenetic phenomena

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Prog Neuro-Psychopharmacol Biol Psychiatry. 2018.

GENETIC IMAGING STUDY WITH [TC-99M] TRODAT-1 SPECT IN ADOLESCENTS WITH ADHD USING OROS-METHYLPHENIDATE.

Akay AP, Kaya G, Kose S, et al.

Aim: To examine theeffects on the brain of 2-month treatment withamethylphenidate extended-release formulation (OROS-MPH) using [Tc-99m] TRODAT-1SPECT in a sample of treatment-na+»ve adolescents with Attention Deficit/Hyperactivity Disorder (ADHD). In addition, to assess whether risk alleles (homozygosity for 10-repeat allele at the DAT1 gene were associated with alterations in striatal DAT availability.

Methods: Twenty adolescents with ADHD underwent brain single-photon emission computed tomography (SPECT) scans with [Tc-99m] TRODAT-1 at baseline and two months after starting OROS-MPH treatment with dosages up to 1 mg/kg/day. Severity of illness was estimated using the Clinical Global Impression Scale (CGI-S) and DuPaul ADHD Rating Scale-Clinician version (ARS) before treatment,1 month and 2 months after initiating OROS-MPH treatment.

Results: Decreased DAT availability was found in both the right caudate (pretreatment DAT binding: 224.76 -¦ 33.77, post-treatment DAT binding: 208.86 -¦ 28.75, p = 0.02) and right putamen (pre-treatment DAT binding: 314.41 -¦ 55.24, post-treatment DAT binding: 285.66 -¦ 39.20, p = 0.05) in adolescents with ADHD receiving OROS-MPH treatment. Adolescents with ADHD who showed a robust response to OROS-MPH (n = 7) had significantly greater reduction of DAT density in the right putamen than adolescents who showed less robust response to OROS-MPH (n = 13) (p = 0.02). However, between-group differences by treatment responses were not related with DAT density in the right caudate. Risk alleles (homozygosity for the 10-repeat allele of DAT1 gene) in the DAT1 gene were not associated with alterations in striatal DAT availability.

Conclusion: Two months of OROS-MPH treatment decreased DAT availability in both the right caudate and putamen. Adolescents with ADHD who showed a robust response to OROS-MPH had greater reduction of DAT density in the right putamen. However,our findings did not support an association between

homozygosity for a 10-repeat allele in the DAT1 gene and DAT density, assessedusing[Tc-99m] TRODAT-1SPECT

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Psychiatry Clin Neurosci. 2018.

EVALUATION OF THE NEUTROPHIL/LYMPHOCYTE RATIO, PLATELET/LYMPHOCYTE RATIO, AND MEAN PLATELET VOLUME AS INFLAMMATORY MARKERS IN CHILDREN WITH ATTENTION-DEFICIT HYPERACTIVITY DISORDER.

Avcil S.

Aim: The neutrophil/lymphocyte ratio (NLR), platelet/lymphocyte ratio (PLR), monocyte/lymphocyte ratio (MLR), and mean platelet volume (MPV) have recently been used as indicators of a systemic inflammatory response. The aim of this study was to investigate the relations of the NLR, PLR, MLR, and MPV with attention-deficit hyperactivity disorder (ADHD).

Methods: The study group consisting of 82 children diagnosed with ADHD was compared with a healthy control (HC) group of 70 age-, sex-, and body-mass-index-matched subjects. The NLR, PLR, MLR, and MPV were measured according to the complete blood count.

Results: The NLR, PLR, MLR, MPV, and neutrophil count of the ADHD group were significantly higher than those of the HC group. The lymphocyte counts of the patients were significantly lower than those of the HC group.

Conclusion: Inflammation might play a role in the etiopathogenesis of ADHD. The NLR, PLR, MLR, and MPV may be potential inflammation markers for ADHD in children

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Psychiatry and Clinical Psychopharmacology. 2018 Mar;28:19-24.

BEHAVIOURAL SLEEP PROBLEMS IN PREVIOUSLY UNTREATED CHILDREN WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER.

Eyuboglu M, Eyuboglu D.

Objective: Although sleep symptoms are not included in the diagnostic criteria of attention deficit hyperactivity disorder (ADHD), these problems are common in children with ADHD. The presence of sleep problems was associated with impairment in functionality and increase in ADHD intensity. The aims of the study were to evaluate sleep problems of children with ADHD who had never received any psychiatric treatment and investigate the effects of these problems in functionality.

Methods: The present study included 83 children who were diagnosed as having ADHD and had never received any psychiatric treatment. The control group consisted of 106 healthy children. Psychiatric diagnostic interview was applied to all children. The parents completed the Conner's Parent Questionnaire to evaluate the intensity of ADHD in the children, the Children's Sleep Habits Questionnaire (CSHQ) to evaluate sleep problems, and the Weiss Functional Impairment Rating Scale to evaluate the functionality of the children.

Results: The total scores of subscale and scales of CSHQ were significantly higher in the study group. ADHD children slept 1 hour later and sleep quantity was 1.5 hours less than the control group. There was a significant correlation between sleep problems, ADHD severity, and functionality of these children.

Conclusions: The results demonstrated that children with ADHD experienced more sleep problems and slept less than the children in the healthy control group, and functional impairments increased due to these problems. Another important finding is that sleep problems are not related to drug use. Maintaining sleep hygiene or interventions against sleep problems may increase sleep quality and may improve self and family functionality. Therefore, the standardized sleep evaluation must be performed in cooperation with parents in all children with ADHD

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Psychiatry and Clinical Psychopharmacology. 2018 Mar;28:80-90.

FACEBOOK OVERUSE AND ADDICTION AMONG TURKISH ADOLESCENTS: ARE ADHD AND ADHD-RELATED PROBLEMS RISK FACTORS?

Gul H, Solmaz EY, Gul A, et al.

Objective: In the last decade, using social network sites (SNSs) has grown and become an integral part of daily routine for adolescents. As known, ADHD is a major public health problem for all addiction types, including the Internet and SNSs addiction. Our aim was to examine the effect of ADHD, impulsivity types, using motivations, internalizing and externalizing symptoms on Facebook (FB) overuse and FB addiction among adolescents.

Methods: Participants were recruited from ADHD and non-ADHD adolescents who were applied to the child and adolescent psychiatry and have an active FB account. We used FB Use and Motivations Form, the Barratt Impulsiveness Scale (BIS), Bergen FB Addiction Scale (BFAS) and Conners-Wells' Adolescent Self-Report Scale-Long form (CASS:L).

Results: Our results indicated that ADHD adolescents have more fake FB accounts, have their own accounts for longer time, are using FB for more motivation types and FB overuse is more frequent than in non-ADHD counterparts. According to the degree of FB use, we have shown that adolescents with FB overuse behaviour have more externalizing symptoms and have higher CASS:L and Barrat impulsivity scores than others. Risk factors for FB overuse are: having a fake FB account and having higher ADHD index scores; risk factors for FB addiction are: higher attentional impulsivity, higher conduct problems scores and higher ADHD index scores.

Conclusions: The results of this study have improved our understanding about the risk factors of a new behavioural addiction type among adolescents

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Psychiatry and Clinical Psychopharmacology. 2018 Mar;28:56-57.

RECREATIONAL ABUSE OF A PRESCRIBED MEDICATION BY AN ADOLESCENT WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER.

Akaltun I, Kara T.

Methylphenidate (MPH) is one of the most commonly used medical therapeutic options in the treatment of attention deficit hyperactivity disorder (ADHD). We discuss a 14-year-old male adolescent started on MPH in therapeutic doses with a diagnosis of ADHD, who then developed euphoria and rapid tolerance, followed by subsequent abuse of medication. The patient and his family both gave written consent for the publication of this report

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Psychiatr Invest. 2018;15:470-75.

THE SYMPTOM TRAJECTORY OF ATTENTION-DEFICIT HYPERACTIVITY DISORDER IN KOREAN SCHOOL-AGE CHILDREN.

Kim KM, Ha M, Lim MH, et al.

Objective We aimed to investigate symptom trajectory of attention-deficit hyperactivity disorder (ADHD) in Korean school-age children.

Methods Four hundred fifty six elementary school children were enrolled when they were in 1st grade and assessed once per year until 4th grade. Symptom severity was assessed by parents using the Korean version of the ADHD rating scale (K-ARS). High-risk was defined as a K-ARS score >18; 377, 325, and 284 children participated in the subsequent assessments. Symptom trajectory was analyzed using a mixed-model approach consistent with the longitudinal nature of the present study including missing data.

Results K-ARS scores demonstrated significant main effects of time ($F=35.33$; $p<0.001$), sex ($F=20.77$; $p<0.001$), and first-year high-risk group ($F=240.90$; $p<0.001$). It also demonstrated a significant time first-year high-risk group interaction effect ($F=38.14$; $p<0.001$), but not a time sex interaction effect.

Conclusion K-ARS scores demonstrated a tendency to decline with aging. Individuals in the high-risk group demonstrated earlier declining tendency than those in the non-high risk group. Although total K-ARS scores differed significantly between the sexes at all assessments, the declining pattern between both sexes did not

differ significantly. Further studies including larger sample sizes, diagnostic inter-views, and complete data sets are needed to confirm findings of the present study

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Psychol Neurosci. 2018;11:95-104.

ATTENTION DEFICIT HYPERACTIVITY DISORDER: BEHAVIORAL REPORT FROM PROFESSORS AND SELF-REPORT FROM UNIVERSITY STUDENTS.

Ramos-Galarza C, Fiallo-Karolys X, Ramos V, et al.

In this article, we analyze the internal consistency of the Diagnostic and Statistical Manual of Mental Disorders–5th ed. (DSM–5) diagnostic criteria for attention-deficit/ hyperactivity disorder (ADHD) in the adult population, in addition, we analyze the correlation between the teacher's report and the student's own, the prevalence of the disorder and the risk of presenting it according to gender. The sample was composed by 175 university students aged between 16 and 36 years old (M 21.49, SD 3.22) that belonged to the private higher education system of Quito, Ecuador. As measurement instruments, two scales were used based on the 18 items of the diagnostic criteria for ADHD described in the DSM–5. As a result, it was determined that the scales used present adequate internal consistency coefficients (attention deficit .77 & .90; hyperactivity/impulsivity .74 & .91 & the total scale .83 & .92 filled by the student and the professor, respectively), all scales correlated significantly between .15 and .88. As far as the ADHD prevalence percentage in university students, findings showed that the subtypes would be present between 7.42% and 26.85% of the time. As a risk factor, it was found that men present more probability to have ADHD than women. The article concludes pointing out the importance to implement intervention programs for university students that could present ADHD, since the condition could influence negatively the spheres in which the students with the disorder perform

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Radiology. 2018 May;287:620-30.

PSYCHORADIOLOGIC UTILITY OF MR IMAGING FOR DIAGNOSIS OF ATTENTION DEFICIT HYPERACTIVITY DISORDER: A RADIOMICS ANALYSIS.

Sun H, Chen Y, Huang Q, et al.

Purpose To identify cerebral radiomic features related to diagnosis and subtyping of attention deficit hyperactivity disorder (ADHD) and to build and evaluate classification models for ADHD diagnosis and subtyping on the basis of the identified features.

Materials and Methods A consecutive cohort of 83 age- and sex-matched children with newly diagnosed and never-treated ADHD (mean age 10.83 years +/- 2.30; range, 7-14 years; 71 boys, 40 with ADHD-inattentive [ADHD-I] and 43 with ADHD-combined [ADHD-C, or inattentive and hyperactive]) and 87 healthy control subjects (mean age, 11.21 years +/- 2.51; range, 7-15 years; 72 boys) underwent anatomic and diffusion-tensor magnetic resonance (MR) imaging. Features representing the shape properties of gray matter and diffusion properties of white matter were extracted for each participant. The initial feature set was input into an all-relevant feature selection procedure within cross-validation loops to identify features with significant discriminative power for diagnosis and subtyping. Random forest classifiers were constructed and evaluated on the basis of identified features.

Results No overall difference was found between children with ADHD and control subjects in total brain volume (1069830.00 mm(3) +/- 90743.36 vs 1079 213.00 mm(3) +/- 92742.25, respectively; P = .51) or total gray and white matter volume (611978.10 mm(3) +/- 51622.81 vs 616960.20 mm(3) +/- 51872.93, respectively; P = .53; 413532.00 mm(3) +/- 41 114.33 vs 418173.60 mm(3) +/- 42395.48, respectively; P = .47). The mean classification accuracy achieved with classifiers to discriminate patients with ADHD from control subjects was 73.7%. Alteration in cortical shape in the left temporal lobe, bilateral cuneus, and regions around the left central sulcus contributed significantly to group discrimination. The mean classification accuracy with classifiers to discriminate ADHD-I from ADHD-C was 80.1%, with significant discriminating features located in the default mode network and insular cortex.

Conclusion The results of this study provide preliminary evidence that cerebral morphometric alterations can allow discrimination between patients with ADHD and control subjects and also between the most common ADHD subtypes. By identifying features relevant for diagnosis and subtyping, these findings may advance the understanding of neurodevelopmental alterations related to ADHD. ((c)) RSNA, 2017 Online supplemental material is available for this article

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Schizophr Bull. 2018;44:S232.

AUDITORY SENSORY GATING IN YOUNG ADOLESCENTS WITH EARLY-ONSET PSYCHOSIS: A COMPARISON WITH ADHD.

Lemvigh C, Jepsen JRM, Fagerlund B, et al.

Background: Numerous studies have demonstrated impaired sensory gating in schizophrenia and this phenomenon has been proposed as a candidate biomarker for the disorder. Sensory gating is typically assessed during an auditory paired-click test commonly referred to as a P50 suppression paradigm. When two identical stimuli are presented, healthy subjects show a decrease in their neural response to the second stimulus, reflected in a decreased P50 amplitude, whereas schizophrenia patients on average show a much smaller decrease. So far, sensory gating has primarily been investigated in adult patients with schizophrenia, but gating disturbances have also been demonstrated in other illnesses, e.g. in schizotypal personality disorder, albeit less marked. Although the typical age of onset for schizophrenia is late adolescence to early adulthood, a sizable group of patients presents with psychotic symptoms during childhood or early adolescence. Manifestation of psychotic symptoms before the age of 18 is commonly referred to as early-onset psychosis (EOP). Various studies have reported a more severe course of illness and a poorer outcome in EOP compared to the adult-onset form of the disorder. In parallel, we expect more pronounced sensory gating deficits in EOP. Impaired sensory gating may not be specific to psychosis, but rather a shared disturbance of neuropsychiatric disorders. Although symptoms of attention deficit hyperactivity disorder (ADHD) differ in many ways from those found in schizophrenia, there are common characteristics. Compared to schizophrenia, relatively few studies have investigated sensory gating in ADHD, and some report P50 gating deficits similar to those frequently found in patients with schizophrenia.

Methods: We investigated P50 suppression in a large cohort of adolescents (12-17 years old) consisting of patients with either EOP (N=56) or ADHD (N=28) as well as age and gender matched healthy controls (N=72). In our paradigm two identical sounds (clicks) were presented separated by a 500ms interval. The amount of suppression was expressed as the ratio between the P50 amplitude of a subject's response to the first click and his/ her amplitude in response to the second click.

Results: The EOP patients scored significantly higher on PANSS (positive, negative, general, and total PANSS scores) compared to both ADHD patients and healthy controls. However, there were neither significant group differences in raw P50 amplitude, nor in the gating ratios between young adolescents with EOP, ADHD and healthy controls.

Discussion: This is the first study to investigate sensory gating in young adolescents with EOP. We found no P50 suppression deficits in these patients which, given the relatively large sample size in our study, cannot merely be ascribed to power issues. The results are in contrast with the majority of studies investigating sensory gating in schizophrenia and ADHD. However, the results are in agreement with earlier studies from our lab showing evidence of inconsistent P50 suppression deficits in two separate cohorts of adult, antipsychotic na+»ve, first-episode patients with schizophrenia. Based on our findings, P50 sensory gating cannot differentiate between young adolescents with EOP or ADHD, and deficient P50 suppression does not seem to be a valid biomarker for EOP

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N-OF-I TRIALS IN CHILD AND ADOLESCENT PSYCHIATRY: A CLOSER LOOK AT STIMULANTS.

Mordijck E, Danckaerts M, Onghena P.

Background: An N-of-i trial is a clinical trial studying the response of an individual to a particular intervention or different interventions in an objective, systematic way.

Aim: To evaluate both the applications and the methodology of N-of-i trials in child and adolescent psychiatry.
Method: A systematic review using PubMed and Embase assessing N-of-i trials published during the period 1986 -July 2016 with the following key-word:'N-of-i'. results 20 articles were induded.AII articles used N-of-itrialstoevaluatetheeffect of stimulant medications in children and adolescents with adho. Most articles recommended the use of the N-of-1 methodology in clinical practice, despite the large variation in methodology and in outcome interpretation of N-of-1 trials.The 20 articles didn't meet the current quality standards for N-of-1 trials.
Conclusion: Despite the advantages of N-of-i trials, the applications in child and adolescent psychiatry turn out to be rather limited and specific. N-of-i trials have more to offer regarding both clinical practice and research in child and adolescent psychiatry. If the methodological recommendations are sufficiently met, N-of-i trials could provide a useful and applicable tool for the child-And adolescent psychiatrist to offer individual patient care

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Trials. 2018;19.

INDIVIDUALISED SHORT-TERM THERAPY FOR ADOLESCENTS IMPAIRED BY ATTENTION-DEFICIT/HYPERACTIVITY DISORDER DESPITE PREVIOUS ROUTINE CARE TREATMENT (ESCAADOL)-STUDY PROTOCOL OF A RANDOMISED CONTROLLED TRIAL WITHIN THE CONSORTIUM ESCALIFE.

Geissler J, Jans T, Banaschewski T, et al.

Background: Despite the high persistence rate of attention-deficit/hyperactivity disorder (ADHD) throughout the lifespan, there is a considerable gap in knowledge regarding effective treatment strategies for adolescents with ADHD. This group in particular often shows substantial psychosocial impairment, low compliance and insufficient response to psychopharmacological interventions. Effective and feasible treatments should further consider the developmental shift in ADHD symptoms, comorbidity and psychosocial adversity as well as family dysfunction. Thus, individualised interventions for adolescent ADHD should comprise a multimodal treatment strategy. The randomised controlled ESCAadol study addresses the needs of this patient group and compares the outcome of short-term cognitive behavioural therapy with parent-based telephone-assisted self-help.
Methods/design: In step 1, 160 adolescents aged 12 to 17 years with a diagnosis of ADHD will undergo a treatment as usual (TAU) observation phase of 1 month. In step 2, those still severely affected are randomised to the intervention group with an Individualised Modular Treatment Programme (IMTP) or a telephone-assisted self-help programme for parents (TASH) as an active control condition. The IMTP was specifically designed for the needs of adolescent ADHD. It comprises 10 sessions of individual cognitive behavioural therapy with the adolescents and/or the parents, for which participants choose three out of 10 available focus modules (e.g. organisational skills and planning, emotion regulation, problem solving and stress management, dysfunctional family communication). TASH combines a bibliotherapeutic component with 10 counselling sessions for the parents via telephone. Primary outcome is the change in ADHD symptoms in a clinician-rated diagnostic interview. Outcomes are assessed at inclusion into the study, after the TAU phase, after the intervention phase and after a further 12-week follow-up period. The primary statistical analysis will be by intention-to-treat, using linear regression models. Additionally, we will analyse psychometric and biological predictors and moderators of treatment response.
Discussion: ESCAadol compares two short-term non-pharmacological interventions as cost-efficient and feasible treatment options for adolescent ADHD, addressing the specific needs and obstacles to treatment success in this group. We aim to contribute to personalised medicine for adolescent ADHD intended to be implemented in routine clinical care

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Trials. 2018;19.

ESCALATE - ADAPTIVE TREATMENT APPROACH FOR ADOLESCENTS AND ADULTS WITH ADHD: STUDY PROTOCOL FOR A RANDOMIZED CONTROLLED TRIAL.

Zinnow T, Banaschewski T, Fallgatter AJ, et al.

Background: Over the last decade, a wide range of attention-deficit/hyperactivity disorder (ADHD) treatment approaches for adults, including both pharmacological interventions and psychosocial treatments, have been proposed and observed to be efficient. In practice, individual treatment concepts are based on results of clinical studies as well as international guidelines (NICE Guidelines) that recommend a step-by-step treatment approach. Since the evidence supporting this approach is limited, the aim of the present study is to determine an optimal intervention regarding severity levels of ADHD symptomatology conducting a randomized controlled trial.

Method: We aim to include 279 ADHD subjects aged between 16 and 45 years. First, participants are randomized to either a face-to-face psychoeducation, telephone assisted self-help (TASH), or a waiting control group (Step 1). All participants assigned to the control group are treated using TASH after a 3-month waiting period. Participants are then allocated to one of three groups, based on their remaining severity level of ADHD symptoms, as (1) full responder, (2) partial responder, or (3) non-responder (Step 2). Full responders receive counseling, partial responders receive either counseling only or counseling and neurofeedback (NF), and non-responders receive either pharmacological treatment only or pharmacological treatment and NF, followed by a 3 month period without intervention.

Discussion: The naturalistic sample is one of the study's advantages, avoiding highly selective inclusion or exclusion criteria. The efficacy of an evidence-based stepped care intervention is explored by primary (reduction of severity of ADHD symptoms) and secondary outcomes (functional outcomes, e.g., quality of life, anger management, enhancement of psychosocial well-being). Predictors of therapeutic response and non-response are being investigated at each step of intervention. Further, sex differences are also being explored

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NEUROPEPTIDE Y LEVELS IN CHILDREN AND ADOLESCENTS WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER.

Bozkurt Ö, Güney E, Göker Z, et al.

Objective: Attention-deficit/hyperactivity disorder (ADHD) is one of the most common psychiatric disorders in adolescence, however, the etiology has not been described. Neuropeptide Y (NPY) is one potential factor that may be involved in the etiology of ADHD. The goal of this study was to evaluate NPY levels in children with ADHD and compare the findings to healthy controls.

Methods: Forty-eight ADHD patients and 40 healthy controls were included in this study. The age range of ADHD patients was 6 to 16 years. All patients were diagnosed according to the fifth edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-V).

Results: The NPY levels of children with ADHD were compared to healthy controls but were not significantly different ($t(86) = -0.887$, $p = 0.378$). NPY levels were similar ($F = 0.191$, $p = 0.826$) between ADHD presentations, and included 8 children with predominantly hyperactive-impulsive type (14.3%), 14 children with predominantly inattentive type (30.4%), and 26 children with a combined type (55.4%). There was also no difference between ADHD patients using medical treatment, ADHD patients not using medical treatment, and control subjects in terms of NPY levels ($F = 0.572$, $p = 0.566$). There was a significant positive correlation between age and NPY levels in the ADHD group ($r = 0.349$, $p = 0.015$).

Conclusion: This study demonstrated that the NPY levels of ADHD subjects were not different than those of controls. Future studies with homogeneous phenotypes and a larger sample population are needed

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EDITORIAL

Are the effects of methylphenidate uncertain?

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Objectives. A recent systematic review and meta-analysis of randomised controlled trials of methylphenidate (MPH) in children and adolescents by a Cochrane group, led by Storebø, raised concern around the level of evidence supporting the use of this medication for attention-deficit/hyperactivity disorder (ADHD) in children and adolescents. This led to several critical responses from a number of ADHD experts.

Methods. This paper reviews the conclusions reached from the Storebø meta-analysis by a critical analysis of methodologies used along with drawing on extant literature.

Results. The controversy raised by the Cochrane meta-analysis should lead to a balanced reflection on the research priorities and needs for the field.

Conclusions. It is hoped the controversy will ultimately lead to improve the quality of the research on the efficacy, effectiveness and tolerability of MPH for ADHD.

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Key words: ADHD, amphetamines, antomoxetine, methylphenidate, stimulants.

Introduction

Whilst several non-pharmacological strategies have been proposed for attention-deficit/hyperactivity disorder (ADHD) (Sonuga-Barke *et al*. 2013; Stevenson *et al*. 2014; Cortese *et al*. 2015, 2016), pharmacological treatment is an important component of the multimodal treatment recommended for this disorder (Cortese *et al*. 2017). Medications for ADHD comprise psychostimulant [e.g. methylphenidate (MPH) and amphetamine derivatives] and non-psychostimulant drugs (e.g. atomoxetine, clonidine and guanfacine) (Cortese & Rosello-Miranda, 2017). MPH is the most commonly used psychostimulant for ADHD in many countries, where it has been used for several decades (Maia *et al*. 2014).

Despite previous systematic reviews and meta-analyses pointing to high effect sizes, when considering the efficacy of MPH for the reduction of ADHD symptoms in the short term (e.g. Schachter *et al*. 2001; Van der Oord *et al*. 2008; Koesters *et al*. 2009; Castells *et al*. 2011), a recent systematic review and meta-analysis by a Cochrane group led by Storebø (Storebo *et al*. 2015) questioned the evidence base for the efficacy and tolerability of MPH for ADHD in children and adolescents. This generated a strong and passionate reaction from the ADHD scientific community (e.g. Banaschewski *et al*. 2016; Romanos *et al*. 2016; Hoekstra & Buitelaar, 2016).

The aim of this paper is to summarise the findings and conclusions of the Cochrane meta-analysis, to present the key critiques to it, and to consider it in the broader context of the evidence base for the efficacy and tolerability of MPH.

The Cochrane meta-analysis

The aim of the work by the Cochrane group led by Storebø was to systematically review and meta-analyse randomised controlled trials (RCTs) reporting outcomes related to the efficacy and/or tolerability of MPH in children and/or adolescents with ADHD. Storebø *et al*. included RCTs of MPH for children and adolescents with ADHD (defined based on DSM-III, III-R, IV, IV-TR, 5 or ICD-9 or 10), with or without psychiatric comorbidities, irrespective of language, publication year, publication type or publication status. Furthermore, it was required that at least 75% of participants in each trial had an IQ >70. The primary outcomes were ADHD symptoms, assessed by teachers. The authors also recorded serious adverse events reported in the studies as a primary outcome, with less severe adverse vents being considered as a secondary outcome measure. Additional secondary outcomes were general behaviour in school and at home, as rated

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by psychometric instruments such as the Child Behaviour Checklist (e.g. CBCL), and quality of life, as measured by psychometric instruments such as the Child Health Questionnaire (e.g. CHQ).

In line with the state of the art recommendations to rate the study risk of bias (RoB) and overall evidence quality, Storebø *et al*. used the Cochrane RoB tool to rate the RoB of individual RCTs included in their systematic review, and the GRADE system to assess the overall quality of the evidence. The standard RoB includes the following six items, which are rated as at low, unclear or high risk for each study: selection bias *(random sequence generation; allocation concealment)*; performance bias *(blinding participants/personnel)*; detection bias *(blinding assessor)*; attrition bias *(incomplete outcome data)*; reporting bias *(selective reporting)*; other bias. Of note, Storebø *et al*. added a 7th item, that is not formally included in the RoB, that is, vested interest, related to industry funding of the study and authors' conflict of interest, in particular due to relationship with drug companies. The authors considered that a study was at overall high RoB if any one of the seven items received a score of either 'high' or 'unclear risk' of bias.

The GRADE system is based on the assessment of the within-trial RoB: directness of the evidence, heterogeneity of the data, precision of effect estimates and risk of publication bias.

Storebø *et al*. found 38 parallel-group trials (including a total of 5111 participants) and 147 cross-over trials (comprising a total of 7134 participants) pertinent for their systematic review. The average duration of the included RCTs was 75 days.

The authors found that the effect size for the efficacy of MPH on the primary outcome (ADHD symptoms rated by teachers) was 0.77 (0.64–0.90), which corresponds to a mean difference (MD) of −9.6 points [95% confidence interval (CI) −13.75 to −6.38] on the ADHD Rating Scale (ADHD-RS). Of note, Storebø *et al*. point out that a change of 6.6 points on the ADHD-RS is considered clinically to represent the minimal relevant difference. The effect size for the primary efficacy measure is indeed one of the highest effect sizes found in psychiatry, and more generally across medical disciplines (Leucht *et al*. 2012).

The authors also found no evidence that MPH was associated with an increase in serious adverse events [risk ratio (RR) 0.98, 95% CI 0.44 to 2.22]. As for the secondary outcomes, teacher-rated general behaviour (SMD −0.87, 95% CI −1.04 to −0.71) and quality of life (SMD 0.61, 95% CI 0.42 to 0.80) were improved with MPH. Regarding secondary outcomes related to tolerability, the authors found a 29% increase in the overall risk of any non-serious adverse events [RR: 0.98, 95% CI 0.44 to 2.22]. The most frequent adverse events were sleep disturbance and appetite decrease. More specifically, children in the MPH group were at 60% greater risk for trouble sleeping/sleep problems (RR 1.60, 95% CI 1.15 to 2.23; 13 trials, 2416 participants), and 266% greater risk for decreased appetite (RR 3.66, 95% CI 2.56 to 5.23; 16 trials, 2962 participants) than children in the control group.

Based on their summative analysis, Storebø *et al*. deemed 'all 185 trials were assessed to be at high risk of bias' and that 'the quality of the evidence was very low for all outcomes'

Therefore, the Cochrane group concluded that 'the low quality of the underpinning evidence means that we cannot be certain of the magnitude of the effects' and that 'If MPH treatment is considered, clinicians might need to use it for short periods, with careful monitoring of both benefits and harms, and cease its use if no evidence of clear improvement of symptoms is noted, or if harmful effects appear'. Finally, Storebø *et al*. recommended the use of nocebo in future studies, to reduce the risk of unblinding.

Critiques to the Cochrane meta-analysis

As mentioned, the Cochrane meta-analysis generated a series of critical reactions from several ADHD experts across the world, both in scientific journals and in blogs, to which Storebø *et al*. have systematically replied.
The main critiques have focused around:

(1) An idiosyncratic and too stringent approach to rate the RoB of individual studies. In particular, it has been highlighted that the RoB in the meta-analysis by Storebø *et al*. included the vested interest item, which is not part of the standard Cochrane RoB (Banaschewski *et al*. 2016). Storebø *et al*. replied that there is evidence, based on work from Andreas Lundh *et al*. (cited in Storebo *et al*. 2015) that 'there are many subtle mechanisms through which sponsorship and conflict of interest may influence intervention effects on outcomes.' However, it has been pointed out (Banaschewski *et al*. 2016) that there is evidence showing that vested interests do not impact the overall RoB of a study. It is fair to conclude that evidence on this issue is far from being conclusive. In addition, it has been highlighted that considering the overall quality of a study as LOW just because at least one item of the RoB was Unclear may be too stringent. Whilst Storebø *et al*. cited evidence supporting this, other meta-analyses (e.g. Catala-Lopez *et al*. 2017), rated the RoB as high if at least one item was rated as high risk; if the risk was rated as 'unclear', this did *not* result in an overall high study RoB. This is important to consider since often times items in the RoB are rated Unclear just because of poor reporting, when indeed the risk could be lower if

full information from the paper were available. Finally, in terms of GRADE, Storebø *et al*. downgraded the quality of evidence by one point for inconsistency of effects (heterogeneity) and by two points for high RoB. Both these decisions are questionable. As for heterogeneity, I^2 for the meta-analysis of the main outcome was 37% for the primary outcome measure. The Cochrane Handbook suggests that heterogeneity up to 40% may not be important. Clearly, there is a certain level of subjectivity and uncertainty in the use of the threshold, which may lead to discrepant views.

(2) Inclusion of studies, such as the Multimodal Treatment of ADHD, with no placebo/no treatment, or studies in pre-schoolers (for which the effects of MPH are notoriously less evident), which is likely to under-estimate the effect of MPH. Although Storebø *et al*. pointed out that this was done according to their pre-published protocol, it goes without saying that issues in the protocol are not less concerning than issues in the meta-analysis *per se*. More importantly, even removing these studies, the assessment of study bias and evidence quality (see previous point) is still problematic.

(3) An emphasis on non-serious adverse events. Indeed, overestimating the adverse events associated with a medication may result in individuals with ADHD being exposed to harm. However, it may lead to the patient not benefitting from effective medications, if the potential adverse events are overestimated, limiting children's access to effective treatment for ADHD, which has serious implications, given the substantial risks of not treating ADHD. Although, as found by Storebø *et al*., sleep disorders and decrease of appetite are more frequent with MPH compared with placebo, they tend to be transitory in most cases and can be clinically managed (Cortese *et al*. 2013), but this was not highlighted in the Cochrane review.

(4) Errors in computation of effect sizes. After the European ADHD Guidelines Group highlighted them, Storebø *et al*. acknowledged these mistakes, stating that they will be corrected in further revisions of the meta-analysis. Overall, these were minor mistakes.

(5) It has been pointed out that the use of a nocebo would be highly unethical in children. Whilst Storebø *et al*. suggested that it should be used initially for adults, the issue of its use in children is still problematic.

Ultimately, it appears that the controversy around the level of the evidence base for MPH is, at least in part, linked to the lack of consensus on how to rate important aspects related to possible RoB of studies and more in the cut off to adopt when using the GRADE to appraise the evidence.

Evidence base for ADHD: the broader context

It should be considered that the duration of the RCTs included in the Cochrane review was overall short (average 75 days), which clearly is not informative for clinicians who see patients usually for many years, given the chronic nature of ADHD in the majority of patients. Overall, readers should consider not only evidence from RCTs, but also from other types of designs and studies. Whilst it is unethical to run RCTs for long periods, it is useful to consider evidence form withdrawal design RCTs (which are still few in the field) and from epidemiological studies. Indeed, large epidemiological studies, published in very high-profile journal, show the long-term benefits of MPH. For instance, a study published in the *New England Journal of Medicine* (Lichtenstein *et al*. 2012) in 25 656 patients with a diagnosis of ADHD found that, compared with non-medication periods, there was a significant reduction of 32% in the criminality rate for men (adjusted hazard ratio, 0.68; 95% CI 0.63 to 0.73) and 41% for women (hazard ratio, 0.59; 95% CI 0.50 to 0.70) when they were treated with MPH. Furthermore, large epidemiological studies have found no evidence for an association between stimulants (including MPH) and severe cardiovascular effects. A large study (Cooper *et al*. 2011) of 1 200 438 children and young adults between the ages of 2 and 24 years found no evidence that current use of a medication for ADHD was associated with an increased risk of severe cardiovascular events (sudden cardiac death, acute myocardial infarction and stroke), although the upper limit of the 95% CI = 0.31 to 1.85) indicated that a doubling of the risk could not be ruled out. Another large study (Habel *et al*. 2011) in 443 198 adults and an additional one (Schelleman *et al*. 2011) in 241, 417 children (3–17 years) concur with the previous one confirming that ADHD drugs use is not associated with increased risk of severe cardiovascular events. Although these large studies are reassuring, a more a recent study found an increased risk of severe cardiovascular events in the first 2 weeks of treatment (Shin *et al*. 2016), although the methodology of this study has been criticised (*BMJ*, 2016).

Finally, when it comes to the evidence on the use of MPH, one should also consider evidence on the neurobiological underpinnings for the action of MPH. Of note, a meta-analysis of functional magnetic resonance imaging studies suggested that MPH normalises brain activity in key brain regions (bilateral inferior frontal cortex/insula) affected in the disorder (Rubia *et al*. 2014).

Overall, readers should consider not only evidence from RCTs, but also from other types of designs and studies.

Conclusions

The meta-analysis by Storebø generated a strong controversy. It appears that some of the issues might be attributed to clinicians' lack of consensus as to the methodology used by the Storebø group and the potential for subjective choices on how each study was rated for both quality and potential bias. It is hoped that the very visible and immediate response to this review, will be an opportunity for the field to think of how to design and conduct better, high quality studies and how to improve the methods to appraise the level of evidence.

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Conflicts of Interest

The author has no conflicts of interest to disclose.

Ethical Standards

The authors assert that all procedures contributing to this work comply with the ethical standards of the relevant national and institutional committee on human experimentation with the Helsinki Declaration of 1975, as revised in 2008.

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(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, n. 778 del 05/02/2015, n. 5954 del 05/12/2016 e N. 1077 del 02/02/2017) Capofila Progetto: UONPIA Azienda Ospedaliera "Spedali Civili di Brescia" "*Percorsi diagnostico-terapeutici per l'ADHD*".

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