NEWSLETTER

INDICE:

ISTITUTO DI RICERCHE FARMACOLOGICHE MARIO NEGRI IRCCS

BIBLIOGRAFIA ADHD GENNAIO 2018

Acad Pediatr. 2018.

RECEIPT OF MEDICATION AND BEHAVIORAL THERAPY AMONG A NATIONAL SAMPLE OF SCHOOL-AGE CHILDREN DIAGNOSED WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.

Walls M, Allen CG, Cabral H, et al.

Objective: In 2011, the American Academy of Pediatrics published practice guidelines for attention-deficit/hyperactivity disorder (ADHD), recommending both medication and behavioral therapy for school-age children. The current study examines associations between child/family characteristics and ADHD medication, behavioral, and combined therapy.

Methods: This study used data from the 2014 National Survey of the Diagnosis and Treatment of ADHD and Tourette syndrome, a nationally representative follow-up survey to the 2011-2012 National Survey of Children's Health. Descriptive statistics were used to estimate frequencies of ADHD treatments and multivariable logistic regression to examine child/family characteristics associated with parent-reported medication use, classroom management, and parent training for children aged 8 to 17 diagnosed with ADHD (n = 2401).

Results: Black and Hispanic children were less likely than white children to have ever received ADHD medication. Hispanic children were less likely than white children to be currently receiving medications (adjusted odds ratio, 0.49; 95% confidence interval, 0.30-0.80). No differences were found in current medication use for black children compared to white children. Thirty-percent of parents reported that their child was currently receiving classroom management, and 31% reported having ever received parent training for ADHD. Children whose ADHD medication was managed by a primary care physician were less likely to receive combined medication and behavioral therapy compared to children managed by specialty physicians (adjusted odds ratio, 2.58; 95% confidence interval, 1.75-3.79).

Conclusions: Most school-age children reported receiving medication for ADHD; however, medication disparities persist. Parent-reported use of behavioral therapies are low. Future research should examine reasons for observed variation in treatment and interventions to optimize ADHD care

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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.

Acta Psychiatr Scand. 2017 Jan;135:8-28.

USE OF PSYCHOTROPIC DRUGS IN PATIENTS WITH AUTISM SPECTRUM DISORDERS: A SYSTEMATIC REVIEW.

Jobski K, Hofer J, Hoffmann F, et al.

OBJECTIVE: The objective of this review was to examine prevalence and patterns of psychopharmacotherapy in individuals with autism spectrum disorder (ASD).

METHOD: A systematic literature search in PubMed, CINAHL, and PsycINFO was performed, including articles published up to November 18, 2015.

RESULTS: A total of 47 studies (data collection: 1976-2012), encompassing >300 000 individuals with ASD, were included. The prevalence of psychopharmacotherapy ranged from 2.7% to 80% (median (overall): 45.7%; median (children): 41.9%; median (adults): 61.5%), with psychotropic polypharmacy occurring in 5.4-54% (median: 23.0%). Regarding drug classes, antipsychotics were most frequently used, followed by attention-deficit/hyperactivity disorder (ADHD) medication and antidepressants. Both older age and psychiatric comorbidity were associated with higher prevalences of psychopharmacotherapy and psychotropic polypharmacy. There were no time trends in psychopharmacotherapy prevalence observable.

CONCLUSION: Despite a lack of pharmacological treatment options for ASD core symptoms, the prevalence of psychopharmacotherapy and polypharmacy in ASD patients is considerable, which is probably due to the treatment of non-core ASD symptoms and psychiatric comorbidities. While there is some evidence for the use of antipsychotics and ADHD medication for these indications, the use of antidepressants should be limited to selected cases

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Addict Behav. 2017 Jan;64:269-74.

CLINICAL VALIDATION OF THE C-VAT 2.0 ASSESSMENT TOOL FOR GAMING DISORDER: A SENSITIVITY ANALYSIS OF THE PROPOSED DSM-5 CRITERIA AND THE CLINICAL CHARACTERISTICS OF YOUNG PATIENTS WITH 'VIDEO GAME ADDICTION'.

van Rooij AJ, Schoenmakers TM, van de Mheen D.

AIMS: Clinicians struggle with the identification of video gaming problems. To address this issue, a clinical assessment tool (C-VAT 2.0) was developed and tested in a clinical setting. The instrument allows exploration of the validity of the DSM-5 proposal for 'internet gaming disorder'.

METHOD: Using C-VAT 2.0, the current study provides a sensitivity analysis of the proposed DSM-5 criteria in a clinical youth sample (13-23years old) in treatment for video gaming disorder (N=32). The study also explores the clinical characteristics of these patients.

RESULTS: The patients were all male and reported spending extensive amounts of time on video games. At least half of the patients reported playing online games (n=15). Comorbid problems were common (n=22) and included (social) anxiety disorders, PDD NOS, ADHD/ADD, Parent-Child relationship problem, and various types of depressive mood problems. The sensitivity of the test was good: results further show that the C-VAT correctly identified 91% of the sample at the proposed cut-off score of at least 5 out of 9 of the criteria. As our study did not include healthy, extreme gamers, we could not assess the specificity of the tool: future research should make this a priority.

CONCLUSION: Using the proposed DSM-5 cut-off score, the C-VAT 2.0 shows preliminary validity in a sample of gamers in treatment for gaming disorder, but the discriminating value of the instrument should be studied further. In the meantime, it is crucial that therapists try to avoid false positives by using expert judgment of functional impairment in each case

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Addict Behav. 2017 May;68:30-34.

ASSOCIATIONS BETWEEN ADVERSE CHILDHOOD EXPERIENCES, STUDENT-TEACHER RELATIONSHIPS, AND NON-MEDICAL USE OF PRESCRIPTION MEDICATIONS AMONG ADOLESCENTS.

Forster M, Gower AL, Borowsky IW, et al.

OBJECTIVE: Few studies have investigated associations between adverse childhood experiences (ACE) and nonmedical use of prescription medication (NMUPM) in population-based samples of adolescents, and

even fewer have examined whether promotive factors might buffer these effects. The present study assesses the direct effects of ACE and positive student-teacher relationships on NUMPD and whether positive student-teacher relationships moderate this association.
DESIGN: Data were from the 2013 Minnesota Student Survey (MSS), an in-school survey administered every three years to students throughout Minnesota. The analytic sample (n=104,332) was comprised of 8th, 9th, and 11th graders.
RESULTS: Approximately 3% of students acknowledged past year NMUPM, the majority of whom reported at least one ACE. The most frequently used prescription drug was Ritalin/ADHD medications (1.71%) followed by opiate-based painkillers (1.67%), tranquilizers (0.92%), and stimulants (0.75%). Students who reported any use tended to use more than one medication. For every additional ACE, there was a 56%, 51%, 47%, and 52% increase in the odds of past year stimulant use, ADHD medication, pain reliever, and tranquilizer use, respectively. The estimated rate of the number of prescription drugs used increased by 62% for every additional ACE. Positive student- teacher relationships buffered the association between ACE and NMUPD, especially at higher levels of ACEs.
CONCLUSION: Our findings have important implications for prevention work. Training educators to recognize trauma symptomology and cultivating strong student-teacher relationships are important considerations for future school-based substance use prevention initiatives

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Addict Behav. 2017 Mar;66:13-16.
SLEEP PATTERNS AND PROBLEMS AMONG EARLY ADOLESCENTS: ASSOCIATIONS WITH ALCOHOL USE.
Marmorstein NR.
INTRODUCTION: Sleep and sleep-related problems are associated with alcohol use and related problems among adults. However, existing research on associations between sleep and alcohol use among early adolescents is minimal, and potential individual and family factors that may affect this association remain largely unexplored. We examined potential associations between frequency of alcohol use and initial insomnia, subjective daytime sleepiness, sleep irregularity, and disturbed sleep among a low-income, ethnic minority sample of early adolescents; we also considered whether psychopathology symptoms and/or parental monitoring accounted for any associations found.
METHODS: 127 youth who participated in the Camden Youth Development Study (64 male; mean age=13.2; 71% Hispanic, 32% African-American) were assessed using self-report measures of sleep, alcohol use, psychopathology symptoms (depressive and conduct disorder), and parental monitoring; in addition, teacher reports of attention-deficit hyperactivity disorder were used.
RESULTS: Initial insomnia and daytime sleepiness (but not sleep irregularity or disturbed sleep) were associated with frequency of alcohol use. The association between initial insomnia and alcohol use remained significant when each form of psychopathology and parental monitoring were adjusted for.
CONCLUSIONS: Among early adolescents, frequency of alcohol use is associated with initial insomnia, even once symptoms of psychopathology and family environment (parental monitoring) are adjusted for. Longitudinal research investigating the direction of this effect and other possible mediators and moderators would be useful in developing preventative and treatment interventions

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Alcohol Clin Exp Res. 2017 Feb;41:334-44.
DIFFERENTIAL RECRUITMENT OF BRAIN REGIONS DURING RESPONSE INHIBITION IN CHILDREN PRENATALLY EXPOSED TO ALCOHOL.
Kodali VN, Jacobson JL, Lindinger NM, et al.
BACKGROUND: Response inhibition is a distinct aspect of executive function that is frequently impaired in children with fetal alcohol spectrum disorders (FASD). We used a Go/NoGo (GNG) task in a functional MRI protocol to investigate differential activation of brain regions in the response inhibition network in children diagnosed with full or partial fetal alcohol syndrome (FAS/PFAS), compared with healthy controls.

METHODS: A rapid, event-related task with 120 Go and 60 NoGo trials was used to study children aged 8 to 12 years-8 with FAS/PFAS, 17 controls. Letters were projected sequentially, with Go and NoGo trials randomly interspersed across the task. BOLD signal in the whole brain was contrasted for the correct NoGo minus correct Go trials between the FAS/PFAS and control groups.
RESULTS: Compared to the FAS/PFAS group, controls showed greater activation of the inferior frontal and anterior cingulate network linked to response inhibition in typically developing children. By contrast, the FAS/PFAS group showed greater BOLD response in dorsolateral prefrontal cortex and other middle prefrontal regions, suggesting compensation for inefficient function of pathways that normally mediate inhibitory processing. All group differences were significant after control for potential confounding variables. None of the effects of prenatal alcohol exposure on activation of the regions associated with response inhibition were attributable to the effects of this exposure on IQ.
CONCLUSIONS: This is the first FASD GNG study in which all participants in the exposed group met criteria for a diagnosis of full FAS or PFAS. Although FASD is frequently comorbid with attention deficit hyperactivity disorder, the pattern of brain activation seen in these disorders differs, suggesting that different neural pathways mediate response inhibition in FASD and that different interventions for FASD are, therefore, warranted

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Alcohol Clin Exp Res. 2017 Jan;41:96-106.
AN ERP STUDY OF RESPONSE INHIBITION IN THE AUDITORY DOMAIN IN CHILDREN WITH FETAL ALCOHOL SPECTRUM DISORDERS.
Gerhold MM, Jacobson SW, Jacobson JL, et al.
BACKGROUND: Previous event-related potential (ERP) studies of response inhibition in children with fetal alcohol spectrum disorder (FASD) have used a visual Go/NoGo task to study the impact of prenatal alcohol exposure on response inhibition. No studies exist using auditory versions of the task; thus, it is unclear how the deficits observed in visual tasks translate into the auditory domain.
METHODS: This study examined ERPs using an auditory Go/NoGo paradigm in a sample of 35 school-age children-18 with heavy prenatal alcohol exposure and 17 normally developing controls.
RESULTS: Alcohol-exposed children performed as well as controls in terms of inhibiting their responses; however, their reaction times were significantly slower under the Go condition. As in the ERP visual Go/NoGo task previously administered to these children, group differences were seen in early perceptual processing, specifically related to stimulus discrimination, with a decrease in P2 amplitude in the alcohol-exposed group. The control group exhibited greater N2 amplitude in the NoGo compared to the Go condition while the alcohol-exposed group did not, suggesting a group difference in the neural substrates underlying conflict monitoring. The alcohol-exposed group demonstrated longer latency P3 with reduced amplitude, suggesting poorer allocation of attention. The alcohol-exposed group also exhibited a late positive component (LPC) similar to the one observed in the previous visual ERP study. This LPC may indicate compensatory neurophysiological function related to resetting of attentional control networks in preparation for the next trial. None of the ERP outcomes in this study were related to potential confounders which included cognitive and socioeconomic measures as well as ADHD diagnosis.
CONCLUSIONS: The observed ERP group differences point to elements of perceptual and attentional processing likely to be involved in the performance deficits often observed in children with FASD. We also observed changes in ERPs related to conflict monitoring/response inhibition, highlighting fetal alcohol-related effects on how the brain responds when there is need to identify and respond to environmental cues by switching away from a prepotent motor response to an inhibited state

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Am J Epidemiol. 2017 Mar;185:317-28.

MATERNAL LICORICE CONSUMPTION DURING PREGNANCY AND PUBERTAL, COGNITIVE, AND PSYCHIATRIC OUTCOMES IN CHILDREN.

Raikkonen K, Martikainen S, Pesonen AK, et al.

Earlier puberty, especially in girls, is associated with physical and mental disorders. Prenatal glucocorticoid exposure influences the timing of puberty in animal models, but the human relevance of those findings is unknown. We studied whether voluntary consumption of licorice, which contains glycyrrhizin (a potent inhibitor of placental 11beta-hydroxysteroid dehydrogenase type 2, the "barrier" to maternal glucocorticoids), by pregnant women was associated with pubertal maturation (height, weight, body mass index for age, difference between current and expected adult height, Tanner staging, score on the Pubertal Development Scale), neuroendocrine function (diurnal salivary cortisol, dexamethasone suppression), cognition (neuropsychological tests), and psychiatric problems (as measured by the Child Behavior Checklist) in their offspring. The children were born in 1998 in Helsinki, Finland, and examined during 2009-2011 (mean age = 12.5 (standard deviation (SD), 0.4) years; n = 378). Girls exposed to high maternal glycyrrhizin consumption (>/=500 mg/week) were taller (mean difference (MD) = 0.4 SD, 95% confidence interval (CI): 0.1, 0.8), were heavier (MD = 0.6 SD, 95% CI: 0.2, 1.9), and had higher body mass index for age (MD = 0.6 SD, 95% CI: 0.2, 0.9). They were also 0.5 standard deviations (95% CI: 0.2, 0.8) closer to adult height and reported more advanced pubertal development (P < 0.04). Girls and boys exposed to high maternal glycyrrhizin consumption scored 7 (95% CI: 3.1, 11.2) points lower on tests of intelligence quotient, had poorer memory (P < 0.04), and had 3.3-fold (95% CI: 1.4, 7.7) higher odds of attention deficit/hyperactivity disorder problems compared with children whose mothers consumed little to no glycyrrhizin (</=249 mg/week). No differences in cortisol levels were found. Licorice consumption during pregnancy may be associated with harm for the developing offspring

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Am J Health Promot. 2017 Mar;31:143-52.

ADVANCING SCHOOL AND COMMUNITY ENGAGEMENT NOW FOR DISEASE PREVENTION (ASCEND).

Treu JA, Doughty K, Reynolds JS, et al.

PURPOSE: To compare two intensity levels (standard vs. enhanced) of a nutrition and physical activity intervention vs. a control (usual programs) on nutrition knowledge, body mass index, fitness, academic performance, behavior, and medication use among elementary school students.
DESIGN: Quasi-experimental with three arms.
SETTING: Elementary schools, students' homes, and a supermarket.
SUBJECTS: A total of 1487 third-grade students.
INTERVENTION: The standard intervention (SI) provided daily physical activity in classrooms and a program on making healthful foods, using food labels. The enhanced intervention (EI) provided these plus additional components for students and their families.
MEASURES: Body mass index (zBMI), food label literacy, physical fitness, academic performance, behavior, and medication use for asthma or attention-deficit hyperactivity disorder (ADHD).
ANALYSIS: Multivariable generalized linear model and logistic regression to assess change in outcome measures.
RESULTS: Both the SI and EI groups gained less weight than the control (p < .001), but zBMI did not differ between groups (p = 1.00). There were no apparent effects on physical fitness or academic performance. Both intervention groups improved significantly but similarly in food label literacy (p = .36). Asthma medication use was reduced significantly in the SI group, and nonsignificantly (p = .10) in the EI group. Use of ADHD medication remained unchanged (p = .34).
CONCLUSION: The standard intervention may improve food label literacy and reduce asthma medication use in elementary school children, but an enhanced version provides no further benefit

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Am J Med Genet A. 2017 Mar;173:647-53.

ANALYSIS OF COPY NUMBER VARIANTS IN 11 PAIRS OF MONOZYGOTIC TWINS WITH NEUROFIBROMATOSIS TYPE 1.

Sites ER, Smolarek TA, Martin LJ, et al.

Phenotypic variability among individuals with neurofibromatosis type 1 (NF1) has long been a challenge for clinicians and an enigma for researchers. Members of the same family and even identical twins with NF1 often demonstrate variable disease expression. Many mechanisms for this variability have been proposed. We have performed an exploratory study of copy number variants (CNVs) as a possible source of phenotypic variability in NF1. We enrolled 11 pairs of monozygotic (MZ) twins with NF1 and their parents, catalogued their clinical characteristics, and utilized a single nucleotide polymorphism (SNP) microarray to identify CNVs in blood and saliva. The 11 twin pairs showed high concordance for presence and number of cafe-au-lait spots, cutaneous neurofibromas, IQ, and ADHD. They were more likely to be discordant for optic pathway glioma, plexiform neurofibromas, skeletal manifestations, and malignancy. Microarray analysis identified a total of 81 CNVs meeting our conservative criteria, 37 of which overlap known genes. Of interest, three CNVs were previously unreported. Microarray analysis failed to ascertain any CNV differences within twin pairs, between twins and parents, or between tissues in any one individual. Results of this small pilot study did not demonstrate any de novo CNV events in our MZ twin pairs, nor were de novo CNVs overrepresented in these individuals with NF1. A much larger sample size would be needed to form any conclusions about the role of CNVs in NF1 variable expressivity. Alternative explanations for discordant phenotypes include epigenetic changes, smaller genetic alterations, or environmental factors

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Am J Orthopsychiatry. 2017;87:62-75.

STABILITY AND CHANGE IN CALLOUS-UNEMOTIONAL TRAITS: LONGITUDINAL ASSOCIATIONS WITH POTENTIAL INDIVIDUAL AND CONTEXTUAL RISK AND PROTECTIVE FACTORS.

Fanti KA, Colins OF, Andershed H, et al.

This longitudinal study examines developmental heterogeneity in callous-unemotional (CU) traits in a large sample of school-age children in Cyprus. Latent Class Growth Analysis revealed 4 trajectory groups of CU traits across 3 time points: stable high, increasing, decreasing, and low. Findings suggested that children in the stable high CU trajectory were more likely to (a) exhibit high and stable levels of conduct problems, attention-deficit/hyperactivity disorder symptoms, impulsivity and narcissism, (b) experience low parental involvement and high parental distress, (c) report low peer support and school connectedness, and (d) score lower on academic performance, executive functioning, social competence, and self-regulation compared to children with low, decreasing, and increasing CU traits. These findings were verified by both parent and child reports. Repeated analysis of variance suggested that increases and decreases in CU traits were associated with similar changes in conduct problems, narcissism, impulsivity, and maternal involvement. Further, children in the decreasing trajectory group were not differentiated from children in the low risk group on measures of executive functioning, academic performance, school connectedness, and peer social support at the last wave of measurement. These findings provide evidence for the importance of taking longitudinal change into account for understanding developmental heterogeneity in CU traits and the association of these traits with possible protective (e.g., stable high maternal involvement) and risk (e.g., decreases in maternal involvement and increases in conduct problems, impulsivity and narcissism) variables

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Am J Psychiatry. 2017 Sep;174:877-85.

ADHD MEDICATION AND SUBSTANCE-RELATED PROBLEMS.

Quinn PD, Chang Z, Hur K, et al.

OBJECTIVE: Substance use disorders are major contributors to excess mortality among individuals with attention deficit hyperactivity disorder (ADHD), yet associations between pharmacological ADHD treatment and substance-related problems remain unclear. This study investigated concurrent and long-term associations between ADHD medication treatment and substance-related events.

METHOD: The authors analyzed 2005-2014 commercial health care claims from 2,993,887 (47.2% female) adolescent and adult ADHD patients. Within-individual analyses compared the risk of substance-related events (i.e., emergency department visits related to substance use disorders) during months in which patients received prescribed stimulant medication or atomoxetine relative to the risk during months in which they did not.
RESULTS: In adjusted within-individual comparisons, relative to periods in which patients did not receive ADHD medication, male patients had 35% lower odds of concurrent substance-related events when receiving medication (odds ratio=0.65, 95% CI=0.64-0.67), and female patients had 31% lower odds of concurrent substance-related events (odds ratio=0.69, 95% CI=0.67-0.71). Moreover, male patients had 19% lower odds of substance-related events 2 years after medication periods (odds ratio=0.81, 95% CI=0.78-0.85), and female patients had 14% lower odds of substance-related events 2 years after medication periods (odds ratio=0.86, 95% CI= 0.82-0.91). Sensitivity analyses supported most findings but were less consistent for long-term associations among women.
CONCLUSIONS: These results provide evidence that receiving ADHD medication is unlikely to be associated with greater risk of substance-related problems in adolescence or adulthood. Rather, medication was associated with lower concurrent risk of substance-related events and, at least among men, lower long-term risk of future substance-related events

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Am J Obstet Gynecol. 2018;218:S461.

MATERNAL HYPOTHYROIDISM INCREASES THE RISK OF ADHD IN THE OFFSPRING.

Getahun D, Fassett MJ, Chiu VY, et al.

OBJECTIVE: To examine if maternal hypothyroidism increases the risk of attention deficit hyperactivity disorder (ADHD) in the offspring and how this risk may be modified by sex, race-ethnicity, and gestational length.
STUDY DESIGN: A retrospective cohort study of singleton born children age 3-11 years delivered at ΓëÑ28 weeks of gestation (n=254,580) in Kaiser Permanente Southern California hospitals (2000-2013) was performed using data abstracted from the Perinatal Service System-«, hospital inpatient, outpatient physician encounter, and pharmacy records. ICD-9 codes from hospitalizations during pregnancy and infant birth certificates as well as pharmacy records on medication specific for ADHD were used to ascertain the exposure and outcomes of interest. Duration of exposure was defined as time interval from first diagnosis until birth and was grouped into quartiles. Adjusted hazard ratios (HR) with 95% confidence interval (CI) were estimated to quantify potential associations between maternal hypothyroidism and child ADHD.
RESULTS: Overall prevalence of hypothyroidism was 2%. Compared with non-ADHD children, ADHD children were more likely to be male and of White or African-American race/ethnicity. Children of women with hypothyroidism were more likely to be diagnosed with ADHD (HR 1.28, 95%CI 1.13-1.44) than offspring of undiagnosed women. A stratified analysis by duration of exposure revealed that exposure length of 2nd and 3rd quartiles were associated with significantly increased risk; 1.41-fold (95%CI 1.12-1.76) and 1.32-fold (95%CI 1.05-1.66), respectively. Hypothyroidism was associated with increased risk of ADHD for Hispanic (HR 1.38, 95%CI 1.14-1.69), African-American, and Other/ Multiple racial/ethnic groups. However, the association for the last two racial groups failed to reach statistical significance. Although boys are four-times as likely as girls to be diagnosed with ADHD, hypothyroidism affect both sex equally.
CONCLUSION: Our results suggest that hypothyroidism is associated with increased risk of childhood ADHD in some ethnic and racial minorities. Maternal hypothyroidism may help identify at-risk children who could benefit from greater surveillance and interventions. Additional studies are also needed to determine if treatment of maternal hypothyroidism may lower the risk of this common neurodevelopmental disorder

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Am J Psychiatry. 2018;175:63-70.

INCREASED RISK OF SMOKING IN FEMALE ADOLESCENTS WHO HAD CHILDHOOD ADHD.

Elkins IJ, Saunders GRB, Malone SM, et al.

Objective: This study examined the effects of childhood attention deficit hyperactivity disorder (ADHD) symptoms, both inattention and hyperactivity-impulsivity, on the development of smoking in male and female adolescents.

Method: Twin difference methods were used to control for shared genetic and environmental confounders in three population-based, same-sex twin samples (N=3,762; 64% monozygotic). One cohort oversampled female adolescents with ADHD beginning in childhood. Regressions of childhood inattentive and hyperactive-impulsive symptoms were conducted to predict smoking outcomes by age 17. ADHD effects were divided into those shared between twins in the pair and those nonshared, or different within pairs.

Results: Adolescents who had more severe ADHD symptoms as children were more likely to initiate smoking and to start smoking younger. The association of ADHD symptoms with daily smoking, number of cigarettes per day, and nicotine dependence was greater in females than in males. Monozygotic female twins with greater attentional problems than their co-twins had greater nicotine involvement, consistent with possible causal influence. These effects remained when co-occurring externalizing behaviors and stimulant medication were considered. Hyperactivity-impulsivity, while also more strongly related to smoking for female adolescents, appeared primarily noncausal.

Conclusions: Smoking initiation and escalation are affected differentially by ADHD subtype and gender. The association of inattention with smoking in female adolescents may be causal, whereas hyperactivity-impulsivity appears to act indirectly, through shared propensities for both ADHD and smoking

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Anesthesiology. 2017 Aug;127:227-40.

ASSOCIATION BETWEEN EXPOSURE OF YOUNG CHILDREN TO PROCEDURES REQUIRING GENERAL ANESTHESIA AND LEARNING AND BEHAVIORAL OUTCOMES IN A POPULATION-BASED BIRTH COHORT.

Hu D, Flick RP, Zaccariello MJ, et al.

BACKGROUND: Exposure of young animals to general anesthesia causes neurodegeneration and lasting behavioral abnormalities; whether these findings translate to children remains unclear. This study used a population-based birth cohort to test the hypothesis that multiple, but not single, exposures to procedures requiring general anesthesia before age 3 yr are associated with adverse neurodevelopmental outcomes.

METHODS: A retrospective study cohort was assembled from children born in Olmsted County, Minnesota, from 1996 to 2000 (inclusive). Propensity matching selected children exposed and not exposed to general anesthesia before age 3 yr. Outcomes ascertained via medical and school records included learning disabilities, attention-deficit/hyperactivity disorder, and group-administered ability and achievement tests. Analysis methods included proportional hazard regression models and mixed linear models.

RESULTS: For the 116 multiply exposed, 457 singly exposed, and 463 unexposed children analyzed, multiple, but not single, exposures were associated with an increased frequency of both learning disabilities and attention-deficit/hyperactivity disorder (hazard ratio for learning disabilities = 2.17 [95% CI, 1.32 to 3.59], unexposed as reference). Multiple exposures were associated with decreases in both cognitive ability and academic achievement. Single exposures were associated with modest decreases in reading and language achievement but not cognitive ability.

CONCLUSIONS: These findings in children anesthetized with modern techniques largely confirm those found in an older birth cohort and provide additional evidence that children with multiple exposures are more likely to develop adverse outcomes related to learning and attention. Although a robust association was observed, these data do not determine whether anesthesia per se is causal

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Arch Clin Neuropsychol. 2017 Dec;32:980-91.

AUDITORY AND VISUAL WORKING MEMORY FUNCTIONING IN COLLEGE STUDENTS WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER AND/OR LEARNING DISABILITIES.

Liebel SW, Nelson JM.

Objective: We investigated the auditory and visual working memory functioning in college students with attention-deficit/hyperactivity disorder, learning disabilities, and clinical controls. We examined the role attention-deficit/hyperactivity disorder subtype status played in working memory functioning. The unique influence that both domains of working memory have on reading and math abilities was investigated.

Method: A sample of 268 individuals seeking postsecondary education comprise four groups of the present study: 110 had an attentiondeficit/hyperactivity disorder diagnosis only, 72 had a learning disability diagnosis only, 35 had comorbid attention-deficit/hyperactivity disorder and learning disability diagnoses, and 60 individuals without either of these disorders comprise a clinical control group. Participants underwent a comprehensive neuropsychological evaluation, and licensed psychologists employed a multi-informant, multi-method approach in obtaining diagnoses.

Results: In the attention-deficit/hyperactivity disorder only group, there was no difference between auditory and visual working memory functioning, $t(100) = -1.57$, $p = .12$. In the learning disability group, however, auditory working memory functioning was significantly weaker compared with visual working memory, $t(71) = -6.19$, $p < .001$, $d = -0.85$. Within the attention-deficit/hyperactivity disorder only group, there were no auditory or visual working memory functioning differences between participants with either a predominantly inattentive type or a combined type diagnosis. Visual working memory did not incrementally contribute to the prediction of academic achievement skills.

Conclusion: Individuals with attention-deficit/hyperactivity disorder did not demonstrate significant working memory differences compared with clinical controls. Individuals with a learning disability demonstrated weaker auditory working memory than individuals in either the attention-deficit/hyperactivity or clinical control groups

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Aust J Psychol. 2017 Dec;69:273-82.

THE IMPACT OF MINDFULNESS MEDITATION TRAINING ON EXECUTIVE FUNCTIONS AND EMOTION DYSREGULATION IN AN IRANIAN SAMPLE OF FEMALE ADOLESCENTS WITH ELEVATED ATTENTION-DEFICIT/HYPERACTIVITY DISORDER SYMPTOMS.

Kiani B, Hadianfard H, Mitchell JT.

Background Mindfulness-based interventions improve a variety of clinical outcomes. Executive functioning (EF) and emotion dysregulation are among the proposed transdiagnostic mechanisms that such interventions are proposed to target. The aim of the current study was to evaluate the impact of mindfulness meditation training on EF and emotion dysregulation in a sample of female adolescents with elevations in attention-deficit/hyperactivity disorder (ADHD) symptoms against a waitlist control condition.

Method This study adopted a mixed 2 (treatment group, waitlist control group) × 2 (pre-test, post-test) design. Adolescent females (13–15 years old) exhibiting elevations in ADHD symptoms according to multiple informants were randomly assigned to a mindfulness treatment group (n = 15) or a waitlist control group (n = 15).

Results Among EF laboratory tasks, planning and inhibition were higher in the treatment group relative to the control group with large effect sizes at post-treatment. The treatment group also exhibited lower scores in self-reported emotion dysregulation (total, nonacceptance of emotional responses, and impulse control difficulties) in comparison to the waitlist control group with large effect sizes at post-treatment. Within group pre-test and post-test comparisons indicated improvement on particular facets of EF and emotion dysregulation only for the treatment group.

Conclusions Mindfulness meditation training improved particular facets of EF and emotion dysregulation in adolescent females with elevations in ADHD symptoms. Treatment development efforts should target clinical populations that exhibit difficulties in these transdiagnostic mechanisms

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Behav Genet. 2017;47:704.

GENOME-WIDE ASSOCIATION STUDY OF EXECUTIVE FUNCTIONS AND THEIR GENETIC RELATIONSHIP WITH IQ, ACADEMIC ACHIEVEMENT AND PSYCHOPATHOLOGY.

Donati G, Dumontheil I, Meaburn E.

Impaired executive function (EF) is associated with increased risk of psychopathology and lower academic achievement. However, relatively little is known about the genetic architecture of EF traits, and the pathways linking genes, cognitive processes and later academic and mental health outcomes. We previously characterized three latent cognitive variables in an adolescent sample; two EF traits (working memory and inhibitory control) and processing speed. We found that each trait explained differing unique variance in maths, English and science as well as DSM V assessments, suggesting that in order to understand specificity in academic and psychological outcomes, an understanding of individual differences at a neurocognitive level is necessary. The goal of the present study was to add to current understanding of the genetics of EF in adolescence and their genetic relationship to psychological and academic outcomes. We performed univariate genome-wide association studies (GWAS) for working memory, inhibition and processing speed (N= 4,817) with adolescents from the Avon Longitudinal Study for Parents and Children. Linkage disequilibrium (LD) score regression was used to estimate the heritability of each trait as well as genetic correlations between our traits and measures of attainment, IQ and psychopathology. A moderate SNP-based heritability estimate was found for WM (0.25) with a smaller estimate for processing speed and IC. Uniformly high (0.66-1.00) genetic correlations were observed for WM and intelligence and educational traits. Moderate to high correlations were found with Anorexia, Depressive Symptoms and ADHD. The picture was more varied for processing speed, as with IC, possibly due to the large standard errors for their heritability estimates. Univariate GWA analyses failed to detect any genome-wide significant associations. However, 50 lead single nucleotide polymorphisms (SNPs) reached suggestive significance, 15 of which are located in genes previously implicated in GWA studies of education, cognition or psychopathology. MAGMA gene analysis showed there to be a higher representation of genes expressed in the brain for WM but not the other traits. The results suggest that WM is highly polygenic trait with links to risk for specific psychopathologies. However it was not clear that studying EF traits is more powerful that studying the end phenotypes themselves

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Behav Genet. 2017;47:690.

A LONGITUDINAL BEHAVIOR GENETIC ANALYSIS OF INHIBITORY CONTROL AND ADHD SYMPTOMS FROM TODDLERHOOD THROUGH EARLY ADOLESCENCE.

Gagne J, Van HC, Lemery-Chalfant K, et al.

Inhibitory control (IC) is a dimension of temperament and an executive function involving the ability to appropriately regulate behavior. In middle childhood, IC is negatively related to non-clinical behavior problems and Attention Deficit Hyperactivity Disorder (ADHD). Multiple twin studies indicate that IC is genetically influenced, however findings depend somewhat on the age of the participants and the assessment methodology (Gagne & Saudino, 2010; 2016; Gagne & Goldsmith, 2011). Parent-ratings of IC show a much more stable and consistent etiology and developmental trajectory than do lab-based assessments. Researchers have also found genetic and environmental covariance between IC and externalizing behavior problems in toddlerhood (Gagne, Saudino & Asherson, 2011) and school age (Lemery-Chalfant, Doelger, Goldsmith, 2008). We examined the development and etiology of IC and ADHD from a multi-method perspective longitudinally from early childhood to adolescence. Participants included 101-245 MZ and 150-424 DZ twin pairs from the Wisconsin Twin Project. Mothers rated IC in todderhood (TBAQ) and first grade (CBQ), and mother ratings of DISC-ADHD symptoms were collected in first grade and again in early adolescence. Phenotypic correlations between IC and ADHD ranged from-.20 to-.68. MZ correlations exceeded DZ correlations, indicating genetic influences. Cross-Twin, cross-Trait correlations for MZ twins exceeded those for DZ twins suggesting genetic covariance between IC and ADHD. Initial bivariate Cholesky decomposition models of toddler IC and first grade ADHD, and first grade IC and early adolescent ADHD yielded genetic and nonshared environmental variances and covariances (genetic correlations between IC and ADHD ranged from-.19-.24). Results show that toddler IC is phenotypically and etiologically associated with ADHD in first grade, as is first grade IC and early adolescent ADHD. Based on these findings,

early IC can be considered a genetic risk factor for later ADHD symptoms. Future analyses will include laboratory-based behavioral assessments of IC in first grade

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Behav Genet. 2017;47:648.

THE ETIOLOGICAL STRUCTURE OF COGNITIVENEUROPHYSIOLOGICAL IMPAIRMENTS IN ADHD IN ADOLESCENCE AND YOUNG ADULTHOOD.

Michelini G, Cheung C, Kitsune V, et al.

Attention-deficit/hyperactivity disorder (ADHD) is associated with multiple cognitive impairments. Previous studies have identified two partially separable familial factors underlying the cognitive impairments in childhood combined-Type ADHD. The extent to which these cognitive impairments share familial influences with ADHD beyond childhood is unknown. Here, we investigate the etiological structure of cognitive-neurophysiological impairments in persistent ADHD in adolescence and young adulthood. In a sample of 356 participants from ADHD and control sibling pairs (11-27 years), factor analyses and multivariate familial models were run on data on IQ, digit span forward (DSF), digit span backward (DSB), and cognitive-performance and event-related potential (ERP) measures from a cued continuous performance task, an arrow flanker task and a fourchoice reaction time task. Three familial factors (cF1-3) were identified, which captured the familial covariation of ADHD with nine cognitive-ERP measures. cF1 loaded on IQ, mean reaction time (MRT) and reaction-Time variability (RTV); cF2 on DSF and DSB; and cF3 on number of errors and ERPs of inhibitory control (NoGo-P3) and error processing (error-related negativity; ERN). All three factors showed significant familial overlap with ADHD (rCF1-ADHD =.50; rCF2-ADHD=-.36; rCF3-ADHD=-.66). Non-familial influences showed the same factor structure, except for IQ that clustered with digit span measures. Non-familial influences on MRT and RTV largely overlapped with those on ADHD, while other non-familial effects were largely measure-specific. By using a broad range of cognitive and neurophysiological measures within a family study, we identified three partially separable familial factors that substantially captured influences shared between cognitive-neurophysiological measures and ADHD in adolescence and adulthood. These results reveal multiple familial and non-familial processes underlying cognitive and brain impairments in persistent ADHD

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Behav Genet. 2017;47:655.

COMMON GENETIC RISK VARIANTS FOR ADHD CONTRIBUTE TO NEURODEVELOPMENTAL AND EXTERNALIZING POPULATION TRAITS.

Brikell I, Larsson H, Yi L, et al .

ADHD is a highly heritable disorder, marked by comorbidity across neurodevelopmental and externalizing conditions. Polygenic risk scores (PRS) for ADHD have previously been shown to predict ADHD clinical case status and ADHD traits in the general population (Martin, Hamshere, Stergiakouli, O'Donovan, &; Thapar, 2014; Stergiakouli et al., 2015). However, it is still unknown to what extent these genetic risk variants are disorder specific, and how they may influence related neurodevelopmental and externalizing traits. We calculated ADHD PRS for 13,471 children from the Child and Adolescent Twin Study in Sweden, using results from the latest iPSYCHsychiatric Genomics Consortium ADHD genome-wide association (GWAS) meta-Analysis. We used confirmatory factor analysis and structural equation modelling to estimate the associations between ADHD PRS and neurodevelopmental and externalizing traits, whilst accounting for covariance across traits. ADHD PRS were significantly associated with elevated levels of trait inattention, impulsivity, autism, learning difficulties, oppositional-defiant and conduct problems. However, only unique associations with impulsivity and conduct problems remained after accounting for cross-Trait covariance via a general latent factor, on which all symptoms loaded positively (loadings=.31-.91, SD=.004-.028). ADHD PRS explained 0.01% (+¦=.10, p=.000) of the variance in the latent general factor, 0.005% (+¦=.073, p=.000) in impulsivity and 0.003% (+¦=.052, p =.035) in conduct problems. We replicated these findings using ADHD PRS based on a GWAS of population ADHD traits. Our results suggest that common genetic variants associated with clinically diagnosed ADHD have pleiotropic effects on neurodevelopmental and externalizing

traits in the general population, which indicate that these associations appear to be largely non-specific. Nonetheless, the ADHD PRS does not only reflect a general liability to childhood neurodevelopmental traits, but also seem to capture genetic risk variants with unique effects on externalizing traits

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Behav Genet. 2017;47:704.

DISENTANGLING GENETIC TRANSMISSION FROM THE ENVIRONMENTAL EFFECT OF MATERNAL DEPRESSION DURING PREGNANCY ON OFFSPRING ADHD.

Norwegian EME, Gjerde LC, Rijsdijk F, et al.

Maternal depression during pregnancy has been associated with ADHD in the offspring. This association may represent a causal effect, where inutero exposure has detrimental consequences for offspring development. However, because the association in general has not been studied with sufficient control for extraneous variables, causal inferences are not justified.Because mothers and their offspring are genetically related, and typically share many aspects of the environment, both pleiotropy and environmental variables not accounted for could be completely, or partially, responsible for the observed association. The aim of the current study is to expand current knowledge by disentangling genetic transmission from the environmental effect of maternal depression during pregnancy on offspring ADHD. We approach the problem using and extended children-of-Twins design, utilizing differential genetic relatedness among sibling mothers and their offspring in order to separate these alternative models for mother-offspring resemblance. Specifically, we will use structural equation models that allows us to quantify and test, genetic and environmental pathways from mother to offspring. The study is part of the Intergenerational Transmission of Risk Project, using data from The Norwegian Mother and Child Cohort Study, a large prospective population-based study of parents and offspring in Norway. Results will be presented at the Conference

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Behav Genet. 2017;47:700.

INTERGENERATIONAL TRANSMISSION OF ADULT TO CHILD ADHD IN A POPULATION-BASED COHORT STUDY.

Ystrom E, Eilertsen E, Rijsdijk F, et al.

Attention deficit hyperactivity disorder (ADHD) is characterized by a persistent pattern of inattention and/or hyperactivity-impulsivity that interferes with functioning. Previous twin and family studies have shown moderate estimates of heritability for adult ADHD and high estimates of heritability of child ADHD. Across these studies, there has been little evidence of substantial effects of environmental factors shared by siblings. However, there is to date comparatively little knowledge on to what extent adult and child ADHD have common genetic risk factors. By using the Intergenerational Transmission of Risk (IToR) study, a twin-family subsample of the Norwegian Mother and Child Cohort study, we will estimate: (1) heritability of adult ADHD, (2) heritability of child ADHD, (3) genetic transmission of adult ADHD to child ADHD, (4) genetic factors specific to child ADHD, and (5) possible direct effects of parental ADHD to child ADHD. To estimate such parameters, we will apply an extended children of twin model on the IToR dataset comprising a large number of sibling/twin families. The results will inform on the biological underpinnings of the similar phenomena of adult and child ADHD. Our estimates of genetic innovation across age is of importance to molecular genetic studies where different age groups are often used in a single sample

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Biomed Pap Med Fac Univ Palacky Olomouc Czech Repub. 2017 Mar;161:75-79.

QUALITY OF LIFE IN PATIENTS WITH GASTROSCHISIS IS COMPARABLE WITH THE GENERAL POPULATION: A QUESTIONNAIRE SURVEY.

Frybova B, Kokesova A, Zemkova D, et al.

AIM: To evaluate long-term quality of life and somatic growth of patients with gastroschisis and compare them with the general population.

METHODS: We performed a questionnaire survey of the quality of life of our patients treated between 2004-2012.
RESULTS: A questionnaire was sent to our 56 patients with gastroschisis, 38 mothers of patients (68%) responded to the questionnaire. 33 of 38 mothers claim that the quality of life of their child is very good, 4 of them responded that it is good. 1 mother confessed that the quality of life was very poor. Anthropometric data show comparable results with the standard population except for patients of 1 year of age who still have lower weight (P<0.001) and body height in the 5th percentile and patients of 3 years of age who are also significantly thinner. 13% of patients in our study group have gastrointestinal problems. 9 patients (24%) attend follow-up at the neurological center (Attention Deficit Hyperactivity Disorder n=6, mental retardation n=1, dysarthria n=2), however, overall intellectual abilities are within normal range. 7 patients underwent surgery for umbilical (n=3) or inguinal hernia (n=4), 2 patients were operated on for undescended testicles, 3 patients were operated on for an adhesive ileus. 92% of mothers are very satisfied with the cosmetic result of the scar.
CONCLUSION: The study has shown that the majority of patients after operation of gastroschisis have a very good quality of life without limitation in comparison with the general population. The presented anthropometric data confirm that the development of patients with gastroschisis is favourable

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Bipolar Disord. 2017 Mar;19:128-34.

ADVERSE EFFECTS OF OBESITY ON COGNITIVE FUNCTIONS IN INDIVIDUALS AT ULTRA HIGH RISK FOR BIPOLAR DISORDER: RESULTS FROM THE GLOBAL MOOD AND BRAIN SCIENCE INITIATIVE.

McIntyre RS, Mansur RB, Lee Y, et al.

BACKGROUND: The burden of illness associated with bipolar disorder (BD) warrants early pre-emption/prevention. Prediction models limited to psychiatric phenomenology have insufficient predictive power. Herein, we aimed to evaluate whether the presence of overweight/obesity is associated with greater cognitive decline in individuals at high risk (HR) or ultra high risk (UHR) for BD.
METHODS: We conducted a retrospective analysis to investigate the moderational role of body mass index (BMI) on measures of cognitive function. Subjects between the ages of 8 and 28 years with a positive family history of BD were compared to age-matched controls with a negative family history of BD. Subjects with at least one biological parent with bipolar I/II disorder were further stratified into UHR or HR status by the presence or absence, respectively, of subthreshold hypomanic, major depressive, attenuated psychotic, and/or attention-deficit/hyperactivity disorder symptoms.
RESULTS: A total of 36 individuals at HR for BD, 33 individuals at UHR for BD, and 48 age-matched controls were included in the analysis. Higher BMI was significantly associated with lower performance on measures of processing speed (i.e. Brief Assessment of Cognition in Schizophrenia-symbol coding: r=-.186, P=.047) and attention/vigilance (i.e. Continuous Performance Test-Identical Pairs: r=-.257, P=.006). There were trends for negative correlations between BMI and measures of working memory (i.e. Wechsler Memory Scale-III Spatial Span: r=-0.177, P=.059) and overall cognitive function (i.e. Measurement and Treatment Research to Improve Cognition in Schizophrenia composite score: r=-.157, P=.097). Negative associations between BMI and cognitive performance were significantly stronger in the UHR group than in the HR group, when compared to controls.
CONCLUSIONS: Individuals at varying degrees of risk for BD exhibit greater cognitive impairment as a function of co-existing overweight/obesity. Prediction models for BD may be substantively informed by including information related to overweight/obesity and, perhaps, other general medical conditions that share pathology with BD. Our findings herein, as well as the salutary effects of bariatric surgery on measures of cognitive function in obese populations, provide the rationale for hypothesizing that mitigating excess weight in individuals at elevated risk for BD may forestall or prevent declaration of illness

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BJOG Int J Obstet Gynaecol. 2018.

ANTIDEPRESSANT USE DURING PREGNANCY AND THE RISK OF ATTENTION-DEFICIT/HYPERACTIVITY DISORDER IN THE CHILDREN: A META-ANALYSIS OF COHORT STUDIES.

Jiang H-Y, Peng C-T, Zhang X, et al.

Background: Evidence for the relationship between antidepressant use during pregnancy and the risk of attention-deficit/hyperactivity disorder (ADHD) in the children is conflicting.
Objective: To assess the association between fetal exposure to antidepressant drugs and the subsequent development of ADHD.
Search strategy: A systematic literature search was conducted in PubMed, EMBASE, PsycINFO, and CINAHL databases to identify relevant cohort studies published from inception until October 2017.
Selection criteria: Cohort studies, identifying children with ADHD diagnosis and linking antidepressant use during pregnancy in their mothers.
Data collection: Two reviewers independently abstracted data and assessed study quality.
Main results: The literature search identified six relevant cohort studies with association between antidepressant exposure during pregnancy and the risk of ADHD in children [hazard ratio (HR) 1.34; 95% confidence interval (CI) 1.14-1.57]. However, the association was not statistically significant when the reference group was mothers with psychiatric disorders not treated during pregnancy (HR 0.96; 95% CI 0.76-1.2; n = 2 studies). Moreover, preconception exposure to antidepressants was significantly associated with increased risk of ADHD (HR 1.82; 95% CI 1.54-2.15; n = 3 studies).
Conclusions: The significant association between antidepressant exposure during pregnancy and ADHD in the children can be partially explained by confounding by indication. Given the low number of included studies, further studies with prospective designs that use validated measurements and controls for important confounders are needed to verify our findings. Tweetable abstract: Antidepressant use during pregnancy may be not associated with ADHD in the offspring

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BMC Pediatr. 2017;17.

CHALLENGES IN DEFINING THE RATES OF ADHD DIAGNOSIS AND TREATMENT: TRENDS OVER THE LAST DECADE.

Davidovitch M, Koren G, Fund N, et al.

Background: There is a global trend of large increases in the prevalence and incidence of Attention Deficit Hyperactivity Disorder (ADHD). This study aimed to address potential causes of these major changes.
Methods: The authors used a large cohort to analyze data employing patients' electronic medical records, with physicians' diagnosis of ADHD, including records of medication purchases.
Results: The prevalence of ADHD diagnoses rose twofold from 6.8% to 14.4% between 2005 and 2014 ($p<0.001$), while the ratio of males to females with ADHD decreased from 2.94 in 2005 to 1.86 in 2014 ($p< 0.001$). The incidence increased, peaking in 2011 before declining in 2014. ADHD medication usage by children and adolescents was 3.57% in 2005 and 8.51% by 2014 ($p< 0.001$).
Conclusions: We report a dramatic increase in the rate of ADHD diagnoses. One of the leading factors to which we attribute this increase is the physicians' and parents' changed attitude towards diagnosing attention/hyperactivity problems, with more parents appear to consider ADHD diagnosis and treatment as a means to improve their child's academic achievements, commonly with the aid of medications. This change in attitude may also be associated with the dramatic increase in female ADHD diagnosis prevalence

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BMC Psychiatry. 2017 Jun;17:208.

SERIOUS CHILD AND ADOLESCENT BEHAVIOUR DISORDERS; A VALUATION STUDY BY PROFESSIONALS, YOUTH AND PARENTS.

Vermeulen KM, Jansen DEMC, Buskens E, et al.

BACKGROUND: In child and youth care, quantitative estimates of the impact of serious behaviour problems have not yet been made. Such input is needed to support decision making on investments in treatment. The

aim of this paper was to elicit valuations of social and conduct disorders in children and adolescents from three different perspectives: professionals, youth, and parents.
METHODS: We obtained valuations from 25 youth care professionals, 50 children (age 9-10) without serious behaviour problems and 36 adolescents (age 16-17) with and without serious behaviour disorders, and 46 parents with children in the aforementioned age categories. Valuations were estimated from 18 descriptions of behaviour disorders in youth aged 9 and 15 years. Descriptions included Oppositional Defiant Disorder (ODD), Conduct Disorder (CD), and Disruptive Behaviour Disorder (DBD). Comorbid conditions were Attention Deficit Hyperactivity Disorder and substance abuse. Valuations were obtained with the EuroQol questionnaire (EQ-5D-3 L) and a visual analogue scale (VAS).
RESULTS: Valuations were generally severe; problems were by and large reported to worsen quality of life by 50% compared to being fully healthy. Professionals regarded DBD with substance abuse as most severe (VAS values 0.41 for children, and 0.43 for adolescents, i.e. less than half of normal). They rated ODD as least severe (VAS values 0.58 for children, 0.59 for adolescents). Children, adolescents and parents gave lower valuations than professionals, and had a wider range of scores, particularly at the lower end of the scale.
CONCLUSIONS: Behaviour disorders pose a formidable burden from the perspectives of professionals as well as children, adolescents and parents. These results may support medical decision making to set priorities with regard to prevention and treatment based on perceived severity

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BMC Psychiatry. 2017 Dec;17.
THE AUTISM–TICS, ADHD AND OTHER COMORBIDITIES INVENTORY (A-TAC): PREVIOUS AND PREDICTIVE VALIDITY.
Mårland C, Lichtenstein P, Degl'Innocenti A, et al.
Background: Reliable and easy to administer screening instruments focusing on neurodevelopmental disorders and associated conditions are scarce. The Autism–Tics, AD/HD and other Comorbidities inventory (A-TAC) has previously been validated and reporting good– excellent validity for several disorders. This article aims to expand these findings by including more conditions in a substantially larger sample augmented with the Swedish National Patient Register (NPR).
Methods: Since 2004 parents of all 9-year-old Swedish twins have been invited to participate in a telephone interview in the Child and Adolescent Twin Study in Sweden, CATSS. The CATSS is linked to the NPR which includes data from in- and outpatient care. Data on neurodevelopmental disorders (A-TAC) collected in CATSS were compared with diagnoses from the NPR. We investigated diagnoses that had been made both before (previous validity) and after (predictive validity) the interview.
Results: Sensitivity and specificity of A-TAC scores for predicting earlier or later clinical diagnoses were mostly good–excellent, with values of the area under the curve for a clinical diagnosis of autism spectrum disorder (ASD) of .98, attention deficit hyperactivity disorder (ADHD) .93, learning disorder (LD) .92, and oppositional defiant disorder (ODD) .99, with small differences in terms of previous and predictive analyses. A-TAC provided little validity for eating disorders.
Conclusion: The result support previous claims: A-TAC is a broad screening instrument with a particular strength in assessing ASD, ADHD, LD, and ODD at ages 9 and 12, and also provides phenotypic information about other child psychiatric disorders

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BMC Psychiatry. 2017 May;17:201.
THE VALIDITY AND PSYCHOMETRIC PROPERTIES OF THE JAPANESE VERSION OF THE COMPULSIVE INTERNET USE SCALE (CIUS).
Yong RKF, Inoue A, Kawakami N.
BACKGROUND: Prolonged Internet use is often associated with reduced social involvement and comorbid psychopathologies, including depression, anxiety, attention-deficit/hyperactivity disorder, and obsessive-compulsive disorder. Asian countries where Internet access is widely available have high reported levels of Internet addiction. As Internet use has changed drastically since concerns about Internet addiction were first

raised, the results of recent studies may be inaccurate because the scales they employed to measure Internet addiction were formulated for different Internet usage from the present. It is thus necessary to develop more-up-to-date scales to assess problematic private use of the Internet.
METHODS: The Compulsive Internet Use Scale (CIUS) was translated into Japanese. An online sample whose ages and sexes reflected that of the national population of Internet users was recruited to test the scale's reliability and validity. Correlations between the scale and Internet-related parameters (such as time spent online, motivation for going online, and applications used) and psychosocial factors (such as psychological distress symptoms and loneliness) were examined. Psychometric properties were examined by the split-half method using both exploratory and confirmatory factor analysis. Model fits were compared across gender.
RESULTS: CIUS was found to have a high reliability and good concurrent, correlation and construct validity. Both exploratory and confirmatory factors revealed that the one-factor solution yielded a satisfactory result across gender. However, the three-factor structural model in which compulsiveness was gauged by "excessive absorption", "difficulty in setting priorities", and "mood regulation" gave the best fit of the model for the general population as well as across gender.
CONCLUSIONS: Compulsive Internet behavior in Japan can be assessed in terms of absorption, priorities, and mood. CIUS is a valid scale for screening compulsive Internet behavior in the general Japanese population regardless of age and gender

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BMC Psychiatry. 2018;18.

ADHD MEDICATION IN OFFSPRING OF IMMIGRANTS - DOES THE INCOME LEVEL OF THE COUNTRY OF PARENTAL ORIGIN MATTER?

Arat A, et al.

Background: Child psychiatric treatment facilities vary greatly worldwide and are virtually non-existent in many low-income countries. One of the most common psychiatric disorders in childhood is ADHD, with an estimated prevalence of 3-5% in Sweden. Previous studies have shown a similar prevalence of ADHD in minority and majority children in Sweden and the UK. However, clinical studies demonstrated that children from immigrant families living in Sweden received less psychiatric care than those of native-born parents. We tested the hypothesis that the consumption of child psychiatric care in immigrant families would be determined by the availability of such treatment in the parents' country of origin. Patterns of medication for attention-deficit hyperactivity disorder (ADHD) were studied as a proxy for child psychiatric care.
Methods: This was a register study of dispensed stimulant medication during 2013-2014 in Swedish national birth cohorts from 1995-2009. The study population, consisting of nearly 1.4 million children, was divided by national income of the parental country of origin and whether the parents were native Swedes, European immigrants, non-European immigrants or a mixture. Logistic regression was used to calculate the odds ratios of having been dispensed at least one ADHD drug during 2013, with adjustments for gender, family status indicating whether the child is living with both parents, household income and area of residence.
Results: Having parents born in low-income (OR [95% confidence interval] 0.27 [0.24-0.29]) or middle-income (European: OR 0.23 [0.20-0.26], non-European: OR 0.39 [0.34-0.41]) countries was associated with lower ADHD treatment levels than having parents born in high-income countries (European: OR 0.60 [0.54-0.66], non-European: OR 0.68 [0.59-0.79]), when compared to children of parents born in Sweden. In families with a background in low or middle income countries, there was no significant association between household income and ADHD medication, while in children with Swedish and mixed backgrounds high level of disposable income was associated with lower levels of ADHD medication.
Conclusion: The use of child psychiatric care by immigrant families in Sweden was largely associated with the income level of the country of origin

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BMC Psychiatry. 2018;18.

EXPERIENCES OF AN INTERNET-BASED SUPPORT AND COACHING MODEL FOR ADOLESCENTS AND YOUNG ADULTS WITH ADHD AND AUTISM SPECTRUM DISORDER -A QUALITATIVE STUDY.

Sehlin H, Hedman AB, Andersson G, et al.

Background: There is a great demand for non-medical treatment and support targeting the needs of adolescents and young adults with autism spectrum disorder (ASD) and attention-deficit/hyperactivity disorder (ADHD). There is also a lack of qualitative studies providing in-depth insight into these individuals' own experiences within this area. The current study aimed to explore how adolescents and young adults with ADHD, ASD or both experienced taking part in an internet-based support and coaching intervention.

Methods: Sixteen participants with ASD, ADHD or both who had participated in an 8-week internet-based support and coaching model, were interviewed using semi-structured interviews. Data was analyzed using qualitative content analysis.

Results: Analysis yielded three themes; Deciding to participate, Taking part in the coaching process and The significance of format. Various motives for joining were expressed by participants, such as viewing the technology as familiar and appealing and expecting it to be better suited to their situation. There was also a previously unfulfilled need for support among participants. In deciding to take part in the intervention the coaches' competence and knowledge were considered essential, often in the light of previously negative experiences. Taking part in the coaching process meant feeling reassured by having someone to turn to in view of shared obstacles to seeking and receiving help. The support was used for talking through and receiving advice on matters related to their diagnosis. Findings further revealed appreciation for aspects relating to the format such as communicating through the written word, being in one's own home and an experience of immediacy. Some disadvantages were voiced including incomplete personal interaction and failing technology. There were also suggestions for greater flexibility.

Conclusions: The in-depth qualitative data obtained from this study suggest that the current model of support and the internet-based format have specific qualities that could play an important role in the support of adolescents and young adults with ADHD and ASD. Although not a replacement for face-to-face interaction, it could be a promising complement or alternative to other support and treatment options

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BMJ. 2017 Jul;358:j2945.

STIMULANT MEDICATION TO TREAT ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.

Santosh P.

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BMJ Open. 2017 Jan;7:e013967.

COMPARATIVE EFFICACY AND TOLERABILITY OF PHARMACOLOGICAL INTERVENTIONS FOR ATTENTION-DEFICIT/HYPERACTIVITY DISORDER IN CHILDREN, ADOLESCENTS AND ADULTS: PROTOCOL FOR A SYSTEMATIC REVIEW AND NETWORK META-ANALYSIS.

Cortese S, Adamo N, Mohr-Jensen C, et al.

INTRODUCTION: Attention-deficit/hyperactivity disorder (ADHD) is a major public health issue. Pharmacological treatments play an important role in the multimodal treatment of ADHD. Currently, there is a lack of up-to-date and comprehensive evidence on how available ADHD drugs compare and rank in terms of efficacy and tolerability, in children or adolescents as well as in adults. We will conduct a network meta-analysis (NMA), integrating direct and indirect comparisons from randomised controlled trials (RCTs), to rank pharmacological treatments for ADHD according to their efficacy and tolerability profiles.

METHODS AND ANALYSIS: We will search a broad range of electronic databases, including PubMed, MEDLINE, EMBASE, PsycINFO, ERIC and Web of Science, with no date or language restrictions. We will also search for unpublished studies using international clinical trial registries and contacting relevant drug companies. We will identify and include available parallel-group, cross-over and cluster randomised trials that compare methylphenidate, dexmethylphenidate, amphetamine derivatives (including lisdexamfetamine), atomoxetine, clonidine, guanfacine, bupropion or modafinil (as oral therapy) either with each other or to

placebo, in children, adolescents or adults with ADHD. Primary outcomes will be efficacy (indicated by reduction in severity of ADHD core symptoms measured on a standardised scale) and tolerability (the proportion of patients who left a study early due to side effects). Secondary outcomes will be global functioning, acceptability (proportion of patients who left the study early by any cause) and changes in blood pressure and body weight. NMA will be conducted in STATA within a frequentist framework. The quality of RCTs will be evaluated using the Cochrane risk of bias tool, and the quality of the evidence will be assessed using the GRADE approach. Subgroup and sensitivity analyses will be conducted to assess the robustness of the findings.
ETHICS AND DISSEMINATION: No ethical issues are foreseen. Results from this study will be published in a peer-reviewed journal and possibly presented at relevant national and international conferences.
TRIAL REGISTRATION NUMBER: CRD42014008976

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Brain Sciences. 2017;7.

EEG DYNAMICS OF A GO/NOGO TASK IN CHILDREN WITH ADHD.

Baijot S, Cevallos C, Zarka D, et al.

Background: Studies investigating event-related potential (ERP) evoked in a Cue-Go/NoGo paradigm have shown lower frontal N1, N2 and central P3 in children with attention-deficit/hyperactivity disorder (ADHD) compared to typically developing children (TDC). However, the electroencephalographic (EEG) dynamics underlying these ERPs remain largely unexplored in ADHD.
Methods: We investigate the event-related spectral perturbation and inter-trial coherence linked to the ERP triggered by visual Cue-Go/NoGo stimuli, in 14 children (7 ADHD and 7 TDC) aged 8 to 12 years.
Results: Compared to TDC, the EEG dynamics of children with ADHD showed a lower theta-alpha ITC concomitant to lower occipito-parietal P1-N2 and frontal N1-P2 potentials in response to Cue, Go and Nogo stimuli, an upper alpha power preceding lower central Go-P3, a lower theta-alpha power and ITC were coupled to a lower frontal Nogo-N3, a lower low-gamma power overall scalp at 300 ms after Go and Nogo stimuli.
Conclusion: These ndings suggest impaired ability in children with ADHD to conserve the brain oscillations phase associated with stimulus processing. This physiological trait might serve as a target for therapeutic intervention or be used as monitoring of their effects

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Cardiol Young. 2017;27:S164.

CARDIOPULMONARY EXERCISE TESTING IN BOYS WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER.

Sielska-Wojtaszek M, Mikulski T, Werner B.

Background: Exercise capacity is one of the most important indicators of health, in children with attention hyperactivity deficit disorder (ADHD) physical activity increases their concentration, cognition, improves motor behavior and exercise tolerance. The aim of the study was to evaluate the exercise capacity of boys with ADHD.
Methods: Cardiopulmonary exercise test (CPET) was conducted in 37 boys with ADHD, (7-17 years, mean 11.3±2.6) who were divided into 3 age subgroups: I - 7-10 years, mean 9.0± 0.3 years, II - 11-13 years, mean 12.1±0.2 years, III - 14-17 years, mean 15.5± 0.4 years. Their results were compared with two age-matched reference groups REF1 (n=68, 8-19 years, mean 14.2±2.9) and REF2 (n=69, 6-17 years, mean 11.5±3.5) of healthy boys.
Results: ADHD boys achieved significantly lower workloads (116 -¦7W) than the healthy boys (REF1-150 ±8W, p<0.01) in the whole group, as well as in the age subgroups (I - 81± 6Wvs. REF1 118 ±9W; II - 114± 5W vs. REF1 140 ±7W, both p< 0.01 and III - 175± 10W vs. REF1 220 ±12 W, p< 0.05). Peak VO2 in ADHD (1.56 ±0.09 l/min) boys was similar to the REF1 values (1.62± 0.08 l/min), but significantly lower than in REF2 (1.92±0.11 l/min, p<0.05). Differential analysis in subgroups showed statistically significant difference only in subgroup II (1.41± 0.08 l/min vs 1.81± 0.09 l/min in REF2, p< 0.01). Anaerobic threshold was achieved at

significantly lower workloads (subgroup I 50 ±3W vs. REF1 86±5W, p <0.001; subgroup II 72± 7W vs. REF1 91 ±8W, p< 0.001). No significant difference in subgroup III was found.
Conclusions: Decreased exercise tolerance was observed in boys with ADHD before their puberty. They reached the anaerobic threshold earlier than their healthy peers, thus the effort is performed less efficiently and associated with greater physiological strain. Cardiopulmonary exercise testing is a safe and valuable diagnostic tool in boys with ADHD

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Child Care Health Dev. 2017 Jan;43:81-88.
CLASSIFYING SENSORY PROFILES OF CHILDREN IN THE GENERAL POPULATION.
Little LM, Dean E, Tomchek SD, et al.
BACKGROUND: The aim of this study was to subtype groups of children in a community sample with and without developmental conditions, based on sensory processing patterns.
METHODS: We used latent profile analysis to determine the number of sensory subtypes in a sample of n = 1132 children aged 3-14 years with typical development and developmental conditions, including autism spectrum disorder (ASD), attention-deficit hyperactivity disorder and learning disabilities.
RESULTS: A five-subtype solution was found to best characterize the sample, which differed on overall degree and differential presentation of sensory processing patterns. Children with and without developmental conditions presented across subtypes, and one subtype was significantly younger in age than others (P < 0.05).
CONCLUSIONS: Our results show that sensory subtypes include both children with typical development and those with developmental conditions. Sensory subtypes have previously been investigated in ASD only, and our results suggest that similar sensory subtypes are present in a sample reflective of the general population of children including those largely with typical development. Elevated scores on sensory processing patterns are not unique to ASD but rather are reflections of children's abilities to respond to environmental demands

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Child Neuropsychol. 2017 Jul;23:554-70.
PARENTAL RATINGS OF DAILY BEHAVIOR AND CHILD COGNITIVE TEST PERFORMANCE AFTER PEDIATRIC MILD TRAUMATIC BRAIN INJURY.
Donders J, DeWit C.
This study aimed to evaluate the degree to which the Behavior Rating Inventory of Executive Function (BRIEF) and Child Behavior Checklist (CBCL) measure overlapping vs. distinct constructs in pediatric patients with mild traumatic brain injury (TBI), and to examine the demographic and injury correlates of such constructs as well as those of cognitive test performance. A total of 100 parents completed the BRIEF and the CBCL within 1 to 12 months after the injury of their child. Groups were contrasted based on the presence vs. absence of impairment on, respectively, the BRIEF and the CBCL. Exploratory maximum likelihood factor analysis was used to evaluate latent constructs. Correlates of the various factor scores were evaluated through regression analysis and contrasted with those of a test of verbal learning and memory. The results revealed that the BRIEF and the CBCL disagree about the presence vs. absence of impairment in about one quarter of cases. A prior history of attention deficit/hyperactivity disorder (ADHD) was associated with an increased likelihood of impairment on both the BRIEF and the CBCL, whereas prior outpatient psychiatric treatment was associated with the increased likelihood of selective impairment on the CBCL. Latent constructs manifested themselves along cognitive regulation, emotional adjustment and behavioral regulation factors. Whereas premorbid characteristics were the exclusive correlates of these factors, performance on a test of verbal learning and memory was negatively affected by intracranial lesions on neuroimaging. It is concluded that the BRIEF and the CBCL offer complementary and non-redundant information about daily functioning after pediatric mild TBI. The correlates of cognitive test performance and parental behavior ratings after such injuries are different and reflect a divergence between premorbid and injury-related influences

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Child Neuropsychol. 2018 Jan;24:61-81.

APPLICATION OF THE DUAL-COMPONENT MODEL OF WORKING MEMORY TO ADHD: GREATER SECONDARY MEMORY DEFICIT DESPITE CONFOUNDED COGNITIVE DIFFERENCES.

Gibson BS, Gondoli DM, Ralph KJ, et al.

The dual-component model postulates that working memory capacity consists of two dissociable components: maintenance in primary memory (PM) and retrieval from secondary memory (SM). Recent application of this model to attention-deficit/hyperactivity disorder (ADHD) has revealed that the SM component is more deficient than the PM component across both verbal and spatial modalities. The present study attempts to strengthen this conclusion by addressing two weaknesses in the previous study. First, the present study shows that the SM component continues to be more deficient than the PM component across both modalities under conditions in which (1) all participants were instructed to use the same recall strategy (resulting in the exclusion of fewer participants); and, (2) individual differences in this strategy were controlled. Second, the present study also documents a group difference in word reading efficiency that is confounded with diagnostic status and that might have influenced estimates of PM and SM capacities in the verbal modality. However, although the SM component is more deficient than the PM component in the ADHD group, the magnitude of this interaction does not vary as a function task modality. These findings are interpreted to suggest that the pattern of WM deficiencies observed are part of a causal pathway that can lead to the symptoms of ADHD, as well as to impairments in reading (and intelligence) due to overlapping cue-dependent retrieval mechanisms. These findings provide additional support for the notion that the SM component of WM is an important and neglected target for treatment

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Child Psychiatry Hum Dev. 2017 Feb;48:18-31.

CALLOUS-UNEMOTIONAL TRAITS AMONG ADOLESCENTS WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER (ADHD): ASSOCIATIONS WITH PARENTING.

Graziano PA, Fabiano G, Willoughby MT, et al.

This study examined the extent to which positive and negative parenting relates to conduct problems (CP) and callous-unemotional (CU) traits among 172 adolescents (72 % males; M(age) = 16.91 years, SD = .67) with attention-deficit/hyperactivity disorder and whether CU traits moderate the link between parenting and CP. Mothers reported on their adolescents' CP, CU traits, and their own parenting practices. Maternal behaviors were observed during a problem-solving communication task. Parents who engaged in more positive parenting (self-reported and observed) reported their adolescents as having lower levels of CU traits. No effect was found for negative parenting. Moderation analyses indicated that lower levels of positive maternal behavior was only associated with higher CP in the presence of higher levels of CU traits. Negative parenting was positively related to CP regardless of CU traits. Positive parenting, irrespective of measurement approach, uniquely relates to adolescents' CU traits while both positive and negative parenting relate to CP

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Clin Chim Acta. 2017 Jul;470:31-35.

IDENTIFICATION OF A NOVEL DE NOVO NONSENSE MUTATION OF THE NSD1 GENE IN MONOZYGOTIC TWINS DISCORDANT FOR SOTOS SYNDROME.

Han JY, Lee IG, Jang W, et al.

INTRODUCTION: Sotos syndrome is a congenital overgrowth disorder characterized by facial gestalt, excessively rapid growth, acromegalic features and a non-progressive cerebral disorder with intellectual disability.

METHODOLOGY: The identical male twins showed somewhat different clinical, cognitive and behavioural phenotypes. Abnormal clinical manifestations including seizures, scoliosis, enlarged ventricles, and attention-deficit/hyperactivity disorder (ADHD) were found in the proband (first twin), but not in the sibling (second twin). We used diagnostic exome sequencing (DES) to identify a heterozygous de novo mutation of the NSD1 gene in monozygotic twins with Sotos syndrome.

RESULTS: DES revealed a novel nonsense mutation c.2596G>T (p.Glu866*) of the NSD1 gene in the proband, the first of monozygotic twins. Sanger sequencing analysis of the proband and his family members showed that this nonsense mutation was present in the proband and his sibling, but was absent in their parents, indicating that it occurred with de novo origin.
CONCLUSION: This finding expands the phenotypic spectrum associated with variable expression of the Sotos syndrome caused by NSD1 mutation, and it adds further support for postconceptual mutation, epigenetic change and/or an environmental factor involved in the cause of the Sotos syndrome

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Clin Neuropsychol. 2017 Nov;31:1353-74.
CHANGING RELATIONS AMONG COGNITIVE ABILITIES ACROSS DEVELOPMENT: IMPLICATIONS FOR MEASUREMENT AND RESEARCH.
Rizeq J, Flora DB, Toplak ME.
OBJECTIVE: The constructs of intelligence and executive function (EF) are commonly used in neuropsychological, cognitive, and developmental research, and in the context of clinical assessment. Yet, we have a limited understanding of the changing age-related associations among these cognitive constructs and the implications for measurement and research. The objectives of this study were to compare hypothetical models using intellectual abilities (non-age corrected scores of intelligence or IQ) and experimental measures of EF and to better understand the role of age in determining the associations between these cognitive abilities at two different periods of development. We also incorporated prediction of ADHD-related difficulties.
METHOD: We examined intellectual abilities and EF in a typically developing child sample (N = 250) and young-adult sample (N = 329). We used confirmatory factor analysis to estimate models for each developmental period: a one-factor model of general cognitive ability and a two-factor model of intelligence and EF. ADHD-related difficulties were regressed on the factors from each model.
RESULTS: Age was more strongly related to all cognitive abilities in the child sample than in the young-adult sample. In the factor analytic models, higher amounts of cognitive test score variance were explained by both models in the child sample than in the young-adult sample. Further, in the child sample, the general cognitive ability factor (combining intellectual abilities and EF) was a significant predictor of ADHD-related difficulties, but the separate intellectual ability and EF factors were not.
CONCLUSIONS: Variables highly associated with age (such as intellectual ability and EF) should not be statistically controlled when assessing cognitive constructs especially in child samples when there is rapid change in cognitive abilities

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Clin Pharmacol Ther. 2017 Dec;102:951-60.
MODEL-BASED APPROACH FOR OPTIMIZING STUDY DESIGN AND CLINICAL DRUG PERFORMANCES OF EXTENDED-RELEASE FORMULATIONS OF METHYLPHENIDATE FOR THE TREATMENT OF ADHD.
Gomeni R, Bressolle-Gomeni F, Spencer TJ, et al.
Methylphenidate (MPH) is currently used to treat children with attention deficit hyperactivity disorder (ADHD). Several extended-release (ER) formulations characterized by a dual release process were developed to improve efficacy over an extended duration. In this study, a model-based approach using literature data was developed to: 1) evaluate the most efficient pharmacokinetic (PK) model to characterize the complex PK profile of MPH ER formulations; 2) provide PK endpoint metrics for comparing ER formulations; 3) define criteria for optimizing development of ER formulations using a convolution-based model linking in vitro release, in vivo release, and hour-by-hour behavioral ratings of ADHD symptoms; and 4) define an optimized trial design for assessing the activity of MPH in pediatric populations. The convolution-based model accurately described the complex PK profiles of a variety of ER MPH products, providing a natural framework for establishing an in vitro/in vivo correlation and for defining criteria for assessing comparative bioequivalence of MPH ER products

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Clin Case Stud. 2018;17:21-37.

THE EFFECTS OF BEHAVIORAL PARENT TRAINING WITH ADJUNCTIVE SOCIAL SKILLS TRAINING FOR A PREADOLESCENT GIRL WITH ADHD AND BORDERLINE PERSONALITY FEATURES.

Babinski DE, Mills SL, Bansal PS.

Girls with attention deficit hyperactivity disorder (ADHD) are at high risk of a range of socialΓÇôemotional difficulties, including peer rejection, suicide attempts, and borderline personality disorder (BPD), which are associated with serious, long-term impairment and have not emerged as clearly in samples of boys with ADHD. BPD is a particularly concerning long-term outcome of ADHD in girls, given the high risk for suicidality and long-lasting relationship difficulties. Very little research has focused on treatment for the interpersonal impairments of girls with ADHD, or on addressing risk for developing BPD. This case study describes the use of behavioral parent training (BPT) with adjunctive social skills training (SST) to address the social–emotional difficulties of a 9-year-old girl, "Violet," who was diagnosed with ADHD Combined Presentation and was being treated with medication for anxiety. Violet presented with many social difficulties, including low self-esteem, emotional dysregulation, and unstable relationships, which were conceptualized as borderline personality features (BPF). Treatment was associated with improvements in parent functioning, including reductions in caregiver strain and inconsistent discipline, as well as improvements in child functioning, including reductions in ADHD symptoms, a range of impairments, and BPF. This case study illustrates the benefit of a brief psychosocial intervention in reducing multiple indices of interpersonal impairment, including BPF, for a girl with ADHD

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Compr Psychiatry. 2017 Jul;76:45-55.

PSYCHOPATHOLOGY AND TRAFFIC VIOLATIONS IN SUBJECTS WHO HAVE LOST THEIR DRIVING LICENSE.

Valero S, Bosch R, Corominas M, et al.

BACKGROUND: The persistence of risky behaviors while driving and traffic accidents despite campaigns to increase awareness suggest that there may be underlying causes that maintain proneness to traffic violations. The aim of the current study was to assess: a) the prevalence of psychopathology in a sample of people who have lost their driving license due to former traffic violations and b) the discriminatory capacity of each psychopathological disorder to differentiate among people with high and low proneness to perform risky behaviors while driving.

METHODS: 383 participants in a course to recover their driving license after its loss due to previous traffic violations were included. The International Neuropsychiatric Interview (M.I.N.I.) according to DSM-IV was used to assess psychopathology.

RESULTS: Between 67% and 76.2% of the participants had been affected by a lifetime psychopathological disorder until the moment of assessment. The most prevalent diagnoses were substance abuse including alcohol (52.5-62.7%), ADHD (19.7-28.5%), depression (7.9-14.4%) and anxiety (3.6-12.4%). Substance abuse and ADHD also showed the strongest set of associations with specific risk behaviors, but ADHD emerged as the most discriminant disorder to distinguish between those people at high and low risk of while driving.

CONCLUSIONS: The results of the current study suggest that addressing psychopathology explicitly to prevent risky behaviors and recidivism while driving would provide benefits in this area

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Compr Psychiatry. 2017 Jul;76:129-37.

THE PROTECTIVE EFFECT OF CHARACTER MATURITY IN CHILD AGGRESSIVE ANTISOCIAL BEHAVIOR.

Kerekes N, Falk O, Brandstrom S, et al.

BACKGROUND: Childhood aggressive antisocial behavior (CD) is one of the strongest predictors of mental health problems and criminal behavior in adulthood. The aims of this study were to describe personality profiles in children with CD, and to determine the strength of association between defined neurodevelopmental symptoms, dimensions of character maturity and CD.

METHODS: A sample of 1886 children with a close to equal distribution of age (9 or 12) and gender, enriched for neurodevelopmental and psychiatric problems were selected from the nationwide Child and Adolescent Twin Study in Sweden. Their parents rated them according to the Junior Temperament and Character Inventory following a telephone interview during which information about the children's development and mental health was assessed with the Autism-Tics, AD/HD and other Comorbidities inventory.

RESULT: Scores on the CD module significantly and positively correlated with scores on the Novelty Seeking temperament dimension and negatively with scores on character maturity (Self-Directedness and Cooperativeness). In the group of children with either neurodevelopmental or behavioral problems, the prevalence of low or very low character maturity was 50%, while when these two problems coexisted the prevalence of low or very low character maturity increased to 70%. Neurodevelopmental problems (such as: oppositional defiant disorder, symptoms of attention deficit/hyperactivity disorder and autism spectrum disorder) and low scores on character maturity emerged as independently significant predictors of CD; in a multivariable model, only oppositional defiant symptoms and impulsivity significantly increased the risk for coexisting CD while a mature self-agency in a child (Self-Directedness) remained a significant protective factor.

CONCLUSION: These results suggest that children's willpower, the capacity to achieve personally chosen goals may be an important protective factor - even in the presence of neurodevelopmental and psychiatric problems - against progressing into persistent negative outcomes, such as aggressive antisocial behaviors

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Dev Cogn Neurosci. 2017 Jun;25:58-68.

CHILDREN'S HEAD MOTION DURING FMRI TASKS IS HERITABLE AND STABLE OVER TIME.

Engelhardt LE, Roe MA, Juranek J, et al.

Head motion during fMRI scans negatively impacts data quality, and as post-acquisition techniques for addressing motion become increasingly stringent, data retention decreases. Studies conducted with adult participants suggest that movement acts as a relatively stable, heritable phenotype that serves as a marker for other genetically influenced phenotypes. Whether these patterns extend downward to childhood has critical implications for the interpretation and generalizability of fMRI data acquired from children. We examined factors affecting scanner motion in two samples: a population-based twin sample of 73 participants (ages 7-12 years) and a case-control sample of 32 non-struggling and 78 struggling readers (ages 8-11 years), 30 of whom were scanned multiple times. Age, but not ADHD symptoms, was significantly related to scanner movement. Movement also varied as a function of task type, run length, and session length. Twin pair concordance for head motion was high for monozygotic twins and moderate for dizygotic twins. Cross-session test-retest reliability was high. Together, these findings suggest that children's head motion is a genetically influenced trait that has the potential to systematically affect individual differences in BOLD changes within and across groups. We discuss recommendations for future work and best practices for pediatric neuroimaging

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Dev Med Child Neurol. 2017;59:57.

PREVALANCE OF ATTENTION DEFICIT HYPERACTIVITY DISORDER AMONG PRIMARY SCHOOL CHILDREN WITH POOR ACADEMIC PERFORMANCE IN THE FCT.

Offiong UM, Mairiga F, Ali I.

Introduction: Poor academic performance can be defined as a school achievement below the expected for a given age, cognitive skill and schooling. Good school performance is associated with future success. Attention Deficit Hyperactivity Disorder (ADHD) is a cause of poor school performance. It affects 8-12% of school aged children worldwide. While ADHD if treated can improve school outcomes, there is limited data on its occurrence in children failing in school, thus the indication for the study.

Materials and Methods: This cross sectional observational study was carried out in 7 public primary schools in Gwagwalada Area council. The inclusion criteria were children who scored below 50% in mathematics, science and English language during two (2) consecutive terms. The instrument was the ADHD Rating Scale-IV-School Version.

Results: A total of 103 forms were returned giving a response rate of 82.4%, one form had no student biodata thus was discarded. There were 44 females and 58 males giving a ratio of 1:1.3. The ages ranged from 8 years to 17 years with a mean age of 11.9 years. There were 50 (48.5%) children assessed to have 6 items or more scoring 2-3 in either the subsets of hyperactivity-impulsivity or inattentiveness; 17(34%) were females and 33(66%) were males. The male to female ratio was 1.94:1. The ADHD subset distribution showed 16 (32%) had combined, 3(6%) had hyperactivity-impulsivity while 31 (62%) had inattentiveness. The inattentive subtype was also the most prevalent subtype across gender and age groups.

Discussion: Poor school performance is regarded as a symptom not a diagnosis as it may be a reflection of a larger problem thus it requires careful investigation. A prevalence of 43% was seen in this study. There is need for further studies to develop policies for intervention to improve education for these chil-dren

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Disabil Rehabil. 2017 Jun;39:1059-72.

AGREEMENTS AND DISAGREEMENTS BETWEEN CHILDREN AND THEIR PARENTS IN HEALTH-RELATED ASSESSMENTS.

Hemmingsson H, Olafsdottir LB, Egilson ST.

PURPOSE: To systematically review research concerning parent-child agreement in health-related assessments to reveal overall agreement, directions of agreement, and the factors that affect agreement in ratings.

METHOD: The Uni-Search and five additional databases were searched. Children's health issues were grouped into psychosocial issues including autism and ADHD, and physical and performance issues including pain. Measures used for comparison were those addressing (a) psychosocial functioning, (b) physical and performance functioning, and (c) health-related quality of life.

RESULTS: Totally, 39 studies met the inclusion criteria, comprising 44 analyses in all since four studies contained more than one analyses. Moderate child-parent agreement was demonstrated in 23 analyses and poor agreement in 20 analyses. Several analyses found more agreement on observable/external than on non-observable/internal domains. Overall, parents considered their children had more difficulties than did the children themselves, although there were indications that for children with physical performance issues, parents may underreport their children's difficulties in emotional functioning and pain. There were no consistencies in differences between children's and parent's ratings on levels of agreement with respect to the children's health issue, age or gender.

CONCLUSIONS: Discrepancies between child and parent reports seem to reflect their different perspectives and not merely inaccuracy or bias. Implications for Rehabilitation In general, parents consider their children to have more difficulties - or more extensive difficulties - than the children themselves think they have. The perspectives of the child and his or her parents should be sought whenever possible since both constitute important information concerning the child s health and well-being. Children with physical and performance issues reported more difficulties than their parents concerning the children's emotional functioning and pain. Clinicians should prioritize obtaining children's views on subjective aspects such as emotional issues as well as on pain

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Drug Alcohol Depend. 2017 Jun;175:1-8.

RELATIONS BETWEEN MENTAL HEALTH DIAGNOSES, MENTAL HEALTH TREATMENT, AND SUBSTANCE USE IN HOMELESS YOUTH.

Narendorf SC, Cross MB, Santa MD, et al.

BACKGROUND: Youth experiencing homelessness have elevated rates of mental illness and substance use compared to the general population. However, the extent to which underlying mental health issues may contribute to substance use as a way to manage symptoms and whether mental health treatment may reduce risk for substance use is unclear. This paper investigated these relations in a community sample of homeless youth.

METHODS: Youth ages 13-24 (N=416) were interviewed as part of a community count and survey of homeless youth in Houston, Texas. A path analysis examined relations among lifetime diagnoses of ADHD, bipolar disorder, and depression; past-month marijuana, alcohol, and synthetic marijuana use, and hypothesized mediators of past-year mental health treatment and perceived unmet need for treatment.

RESULTS: Rates of prior mental disorder diagnoses were high, with extensive comorbidity across the three diagnoses (n=114, 27.3% had all three diagnoses). Relations varied by diagnoses and substances. ADHD was positively related to current marijuana use (beta=0.55 (0.16), p<0.001), a relation that mental health treatment did not mediate. Depression was positively related to synthetic marijuana use through unmet need (beta=0.25 (0.09), p=0.004) and to alcohol use through unmet need (beta=0.20 (0.10), p=0.04)

CONCLUSIONS: This study provides new information about relations between prior mental health diagnoses and substance use in homeless youth. Findings support the need to consider prior mental disorder diagnoses in relation to current substance use and to assess for whether youth perceive they have unmet needs for mental health treatment

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Drugs and Therapy Perspectives. 2018;34:43-49.

METHYLPHENIDATE EXTENDED-RELEASE ORALLY DISINTEGRATING TABLETS (COTEMPLA XR-ODT) IN ATTENTION-DEFICIT HYPERACTIVITY DISORDER IN CHILDREN AGED 6-17 YEARS: A PROFILE OF THEIR USE.

Lyseng-Williamson KA.

The extended-release orally disintegrating tablet (XR-ODT) formulation of methylphenidate (Cotempla XR-ODT) is an effective and generally well-tolerated option for the treatment of attention-deficit hyperactivity disorder (ADHD) in children and adolescents. Because of the pharmacokinetic profile of this formulation, methylphenidate XR-ODT is administered once daily. As methylphenidate XR-ODT comprise both immediate- and extended-release methylphenidate particles, its use may be of particular benefit in individuals who require a rapid onset (clinical improvements are shown within 1-h) and prolonged reduction in ADHD symptoms (clinical improvements are maintained for 12-h). The XR-ODT formulation of methylphenidate allows relatively easy administration (the ODT dissolves rapidly on the tongue, followed by swallowing of the disintegrated particles with saliva without the need for water), which may be of particular benefit in children and adolescents who have difficulty swallowing tablets or capsules

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Dusunen Adam. 2017;30:391-92.

DIAGNOSTIC CONFOUNDING: IS IT ABSENCE EPILEPSY OR ADHD?

Gunes S.

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Early Hum Dev. 2017 Jan;104:7-12.

POPULATION BASED REPORT ON HEALTH RELATED QUALITY OF LIFE IN ADOLESCENTS BORN VERY PRETERM.

Natalucci G, Bucher HU, Von RM, et al.

BACKGROUND: As the survival rate of preterm infants constantly improves, knowledge on the impact of prematurity on long-term health-related quality of life (HRQoL) is important for clinical and parental guidance. We aimed to assess HRQoL in a national cohort of young adolescents born very preterm, and to identify predictors for poorer HRQoL.

PATIENTS AND METHODS: All surviving Swiss live-born children below 30weeks of gestation during the year 2000 (290 subjects) were contacted at age 12years, together with their parents (262 families). HRQoL of the study children was assessed using both the Kidscreen-27 (KS-27) self- and parent forms. Neonatal data of the cohort were prospectively collected.

RESULTS: Among the contacted families, 176 returned the complete set of questionnaires for 194 adolescents (67%): 100 (51%) females, mean (range) gestational age was 27.8 (24.1-29.9) weeks, birth weight 1025 (420-1730) grams, mean age at assessment 12.0 (11.0-13.0) years. Included children had similar neonatal and socio-demographic characteristics as non-responders. Average self- and parent-reported HRQoL of former preterms was similar to Swiss KS-27 norms. According to the multivariable models (r(2)=0.2), surgical closure of patent ductus arteriosus, attention deficit/hyperactivity disorder, severe neurodevelopment impairment were negatively associated with both self- and parent-reported HRQoL.

CONCLUSIONS: HRQoL in this population-based cohort of adolescents born very preterm is good. Surgical closure of patent ductus arteriosus, attention deficit/hyperactivity disorder, severe neurodevelopment impairment were identified as predictors of poorer HRQoL using multivariable models, explaining however only a low proportion of variance in HRQoL

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East J Med. 2017;22:137-42.

EVALUATION OF THE HAND ANTHROPOMETRIC MEASUREMENT IN ADHD CHILDREN AND THE POSSIBLE CLINICAL SIGNIFICANCE OF THE 2D:4D RATIO.

Buru E, et al.

Attention deficit/hyperactivity disorder (ADHD) is characterized with decreased storage time of the information related to the lack of attention and behavioral changes such as hyperactivity and anxiety with hand features. Our purpose was to investigate the possibility to use the 2D:4D ratio in clinics as an easy prediagnostic parameter. A total of 540 people (104 ADHD, 436 controls) between 7-17 years old were included in our study. Our study group revealed a statistically meaningful difference between the ADHD and their controls in 2D:4D ratio of their right hand and the 2D:4D and 4D:5D ratios of their left hand. The male ADHD subjects and controls also demonstrated significant difference in their 2D:4D, 2D:5D, 3D:4D, and 3D:5D ratios of the right hand and the 2D:4D and 2D:5D ratios of the left hand. Especially, ADHD boys had a more feminized 2D:4D left hand ratio than the controls. While, there was a significant difference in all finger ratios of the right hand and the 2D:4D and 4D:5D ratios of the left hand between the ADHD girls and their controls. Thus, the more masculine 2D:4D right hand ratio was observed in ADHD girls. Our results pointed out that the ADHD and some other child psychiatric disorders could be early diagnosed related to the anthropologic parameters. So, the treatment of these individuals could be assigned in early period

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Environmental Pollution. 2018;235:141-49.

RELATIONSHIP BETWEEN BISPHENOL A EXPOSURE AND ATTENTION-DEFICIT/ HYPERACTIVITY DISORDER: A CASE-CONTROL STUDY FOR PRIMARY SCHOOL CHILDREN IN GUANGZHOU, CHINA.

Li Y, Zhang H, Kuang H, et al.

Bisphenol A (BPA) is an endocrine-disrupting chemical. Studies have shown that the exposure to BPA is associated with attention-deficit/hyperactivity disorder (ADHD) during adolescent development. However the direct clinical evidence is limited. To investigate the possible association between environmental BPA exposure and the altered behavior of children, a case-control study was conducted with children aged 6-12

years in Guangzhou, China. Two hundred fifteen children diagnosed with ADHD and 253 healthy children from Guangzhou were recruited as the case and control groups, respectively. Urinary BPA and 8-hydroxy-2'-deoxyguanosine (8-OHdG, a biomarker of oxidative DNA damage) concentrations were determined by high-performance liquid chromatography/tandem spectrometry. The results showed that concentrations of urinary BPA for the case group were significantly higher than those for the control group (3.44 vs 1.70 μg/L; 4.63 vs 1.71 μg/g Crt. $p < .001$). A stepwise increase in the odds ratios for ADHD was observed with the increasing quartiles of children's urinary BPA (first quartile: reference category; second quartile adjusted OR: 1.79, 95% CI: 0.95-3.37; third quartile adjusted OR: 7.44, 95% CI: 3.91-14.1; fourth quartile adjusted OR: 9.41, 95% CI: 4.91-18.1). When the BPA levels were stratified by gender, the odds of ADHD among boys and girls increased significantly with urinary BPA concentrations (adjusted OR: 4.58, 95% CI: 2.84-7.37; adjusted OR: 2.83, 95% CI: 1.17-6.84). Urinary 8-OHdG concentrations in the ADHD children were significantly higher than those in the control group. Furthermore, the linear regression analysis results indicated that a significant relationship existed between BPA exposure and 8-OHdG levels ($R = 0.257$, $p < .001$). Our findings provide direct evidence that childhood BPA exposure may be related to ADHD and 8-OHdG concentrations for children. Moreover, BPA exposure could increase the higher occurrence of ADHD for boy than for girls

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Environnement, Risques et Sante. 2017;16:539-40.

EFFECTS OF PHTHALATE EXPOSURE ON INTELLECTUAL AND ATTENTIONAL PERFORMANCE AT AGE 6.

Nicolle-Mir L.

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Epilepsia. 2017;58:S48.

THE IMPACT OF THE EEG FINDINGS ON THE STRATEGY OF TREATMENT IN CHILDREN WITH ADHD.

Zaytsev I, Zaytsev D, Titov N.

Purpose: According to the literature approximately 15% children with ADHD have certain epileptic activity in long-term sleep EEG. In available literature we couldn't find publications about the impact of EEG findings on ADHD therapy strategy. To determine paroxysmal EEG abnormalities in children with pure ADHD and treatment strategy depending on EEG paroxysmal disturbances.

Method: We've examined 28 children aged 6-10 years with ADHD (DSM-5 classification), without epilepsy and speech development delay. All children were conducted neurological and psychiatric examination, speech therapist examination and long-term sleep EEG recording. All children underwent neuroimaging (CT, MRI) without any disturbances. According to the EEG findings all children were divided into 2 groups: group I (18 children) with epileptic activity, hypnagogic hypersynchrony and it's abnormal variants (with sharp waves on it); group II (10 children) with normal EEG.

Results: Traditional drug methods of ADHD treatment showed significant clinical improvement only in the group II.

Conclusion: Paroxysmal activity in EEG could be the reason for insufficient effect of traditional ADHD treatment

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Epilepsia. 2017;58:S70.

THE CONTRIBUTIONS OF COGNITIVE ABILITIES TO ACADEMIC PROFILE IN NEW-ONSET CHILDHOOD ABSENCE EPILEPSY.

Cheng D, Qian C, Yan X, et al.

Purpose: Neuropsychological studies indicate that new-onset childhood absence epilepsy (CAE) is associated with deficits in attention and executive functioning. However, the contribution of these deficits to impaired academic performance remains unclear. We aimed to examine whether attention and executive function deficits account for the academic difficulties prevalent in patients with new-onset CAE.

Method: Neuropsychological tests were used to assess the cognitive performance in several domains, including language, mathematics, psychomotor speed, spatial ability, memory, intelligence, attention, and executive functioning, in 35 children with new-onset CAE and 33 control participants. One-way analysis of variance (ANOVA) compared performance on all tests between the new-onset CAE group and the control group. Analysis of covariance (i.e., ANCOVA) was conducted to examine the relationships among general cognitive processing, language processing, and mathematical abilities.
Results: Patients with new-onset CAE exhibited deficits in mathematics, intelligence, attention, and executive functioning. They showed preserved performance in language, psychomotor speed, spatial ability and memory. Furthermore, attention deficits, as measured by a visual tracing task, accounted for impaired arithmetic performance in the CAE group.
Conclusion: Children with new-onset CAE exhibit deficits in attention and executive functioning, and is associated with impaired academic performance in mathematics Attention deficits, rather than impaired intelligence or executive functioning, is the fundamental cognitive mechanism underlying mathematical performance impairments in patients with newonset CAE

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Epilepsia. 2017;58:S49-S50.

HIGH PREVALENCE OF INTELLECTUAL DISABILITY, AUTISM, ADHD AND DIMINISHED ADAPTIVE FUNCTIONING IN DOOSE SYNDROME (MAE).

Tang S, Smith A, Parker A, et al.

Myoclonic astatic epilepsy (MAE) is a rare childhood epilepsy with unclear neurodevelopmental outcome. We aimed to deeply phenotyped MAE patients utilising a series of standardised neuropsychological tests. Patients with MAE were recruited from UK paediatric neurology centres from 2012 to 2016. Cases were assessed using the WPPSI III or Bayleys III for cognition; Developmental, Dimensional and Diagnostic Interview (3di) and/or Social Communication Questionnaire (SCQ) for autism spectrum disorder (ASD); the Conner's Comprehensive Behavioural Rating Scale (CBRS) for attention deficit hyperactivity disorder (ADHD) (defined as T score > 70); the Strength and Difficulties questionnaire (SDQ) for behavioural screening; and Adaptive Behaviour Assessment system (ABAS) for adaptive functional skills. 67 (49 Male, 18 Females) MAE cases were recruited. The mean age of seizure onset was 33.9 (SD 14.8) months, and mean age at recruitment was 97.3 (SD 48.4) months. Seizure types were remarkably similar to previous published cohorts. Cognitive testing showed moderate to severe intellectual disability (IQ< 55) in 10/25 (40%), and 4/25 (16%) with mild intellectual disability (IQ 55-70). ASD symptoms were elicited in 20/64 (31.2%) cases through the 3di (9/22) and SCQ (16/61). Parents reported ADHD on the CBRS in 21/52 (41.1%) cases, with 7/52 (13.4%) reaching threshold for both parent and teacher CBRS ($P < 0.0001$). In the SDQ, high or very high scores were recorded in: conduct problems (19/60, $P < 0.0001$), hyperactivity (22/60, $P < 0.0001$), peer problems (26/60, $P < 0.0001$), prosocial problems (29/60, $P < 0.0001$) and psychosocial impact scores (35/60, $P < 0.0001$) compared to a normative population. In the ABAS, 36/59 (61.0%) reported extremely low adaptive scores (< 2nd centile) for conceptual, 25/59 (42.3%) for social and 42/59 (71.1%) for practical domains. These findings reveal a surprisingly high severity and impact of neurodevelopmental comorbidity in MAE and highlight the need for comprehensive evaluation and continued monitoring to guide intervention

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Epilepsia. 2017;58:S185-S186.

RISK FACTORS FOR NEUROPSYCHOLOGICAL IMPAIRMENT IN BENIGN EPILEPSY WITH CENTROTEMPORAL SPIKES.

Almashmoom I, Al-Shuker O, Macdonald D, et al.

Purpose: This study evaluates risk factors for neuropsychological impairment in benign epilepsy with centrotemporal spikes (BECTS).
Method: In a retrospective cohort of 36 children with BECTS, we compared the electroclinical features of 25 who were neuropsychologically normal (Group1) and 11 who developed impairments (Group2) consisting of hyperactivity and attention deficit disorder in all 11 with additional language disturbances in 6.

Results: Median onset age was younger in Group2 than Group1 (4 vs. 8 years), and median epilepsy duration was longer (6.5 vs. 2 years) ($p < 0.001$). Most patients with onset age < 5 years and especially those with >5-year duration were in Group2, while most patients with onset age >5 years and < 5-year duration fell into Group1 ($p < 0.001$). A greater proportion of Group2 took >1 anticonvulsant (36% vs. 4%, $p < 0.05$). Classical or atypical benign epileptiform discharges of childhood (BEDC) were frequent in both groups, but were the only EEG abnormality in half of Group1 vs. none of Group2 ($p < 0.01$). A greater proportion of Group2 had multiregional epileptiform abnormalities (73% vs. 8%), regional intermittent slow activity (91% vs. 16%), or both (73% vs. none) ($p < 0.001$).
Conclusion: Possible risk factors for neuropsychological impairments in BECTS include onset age < 5 years, >5-year epilepsy duration, taking >1 anticonvulsant, multiregional epileptiform abnormalities, and regional intermittent slow activity. Features against these complications may include onset age >5 years and EEG disclosing only BEDC. Risk factor identification might guide potentially beneficial cognitive and educational intervention

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Epilepsia. 2017;58:S153.

EEG FINDINGS IN ATTENTION DEFICIT HYPERACTIVITY DISORDER DISEASE.

AkdaÃ G, et al.

Purpose: Attention deficit hyperactivity disorder (ADHD) is one of the most common psychiatric disorder in childhood and adolescence. The incidence of epilepsy in ADHD is 5-6% and it is seen more common than normal populations. Epileptiform abnormalities on electroencephalography (EEG) were detected in 5-60% of cases.We aimed to investigate the EEG findings in patients with ADHD in this study.
Method: We investigated the EEG reports of the patients whom diagnosed with ADHD during January-December 2016, retrospectively.
Results: We detected 13 patients with ADHD whom underwent EEG examination, of them 5 were female and 8 were male. The mean age of the patients was 11.8 (minimum: 7, maximum: 18). EEG findings; Focal epileptiform foci were found in 4 (30.7%) patients, focal organisation disorder in 3 (23.0%) patients, generalized organisational disorder in 2 (15.3%) patients and generalized epileptiform abnormality were in 1 patient (7.6%). Epileptiform disorder was detected in 30.7% of the patients and 38.4% of the patients had organisation disorder on EEG without clinical symptom. One (8.3%) patient was diagnosed as absence epilepsy because of clinical episodes accompanied by EEG findings.
Conclusion: Epileptic disorders may be the underliying cause in attention disorders. Our findings in ADHD were similar to the literature. However, extensive series of studies are needed

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Epilepsy Behav. 2017 Apr;69:153-60.

TREATMENT ISSUES FOR CHILDREN WITH EPILEPSY TRANSITIONING TO ADULT CARE.

Nabbout R, Camfield CS, Andrade DM, et al.

This is the third of three papers that summarize the second symposium on Transition in Epilepsies held in Paris in June 2016. This paper focuses on treatment issues that arise during the course of childhood epilepsy and make the process of transition to adult care more complicated. Some AEDs used during childhood, such as stiripentol, vigabatrin, and cannabidiol, are unfamiliar to adult epilepsy specialists. In addition, new drugs are being developed for treatment of specific childhood onset epilepsy syndromes and have no indication yet for adults. The ketogenic diet may be effective during childhood but is difficult to continue in adult care. Regional adult epilepsy diet clinics could be helpful. Polytherapy is common for patients transitioning to adult care. Although these complex AED regimes are difficult, they are often possible to simplify. AEDs used in childhood may need to be reconsidered in adulthood. Rescue medications to stop prolonged seizures and clusters of seizures are in wide home use in children and can be continued in adulthood. Adherence/compliance is notoriously difficult for adolescents, but there are simple clinical approaches that should be helpful. Mental health issues including depression and anxiety are not always diagnosed and treated in children and young adults even though effective treatments are available. Attention deficit

hyperactivity disorder and aggressive behavior disorders may interfere with transition and successful adulthood but these can be treated. For the majority, the adult social outcome of children with epilepsy is unsatisfactory with few proven interventions. The interface between pediatric and adult care for children with epilepsy is becoming increasingly complicated with a need for more comprehensive transition programs and adult epileptologists who are knowledgeable about special treatments that benefit this group of patients

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Eur Child Adolesc Psychiatry. 2017 Jul;26:847-56.

IN UTERO EXPOSURE TO BETA-2-ADRENERGIC RECEPTOR AGONIST AND ATTENTION-DEFICIT/HYPERACTIVITY DISORDER IN CHILDREN.

Liang H, Chen J, Miao M, et al.

We aimed to examine the association between in utero exposure to beta2AA and risk of attention-deficit/hyperactivity disorder (ADHD). We established a cohort of 672,265 children born from 1998 to 2008 in Denmark. Children were categorized as exposed if their mothers had redeemed a prescription of beta2AA in pregnancy (from 30 days prior to conception until delivery). We identified children diagnosed with ADHD in the Danish National Hospital Register for the first time after his/her third birthday. Log-linear Poisson regression was used to estimate adjusted incidence rate ratio (aIRR) of ADHD. In total, 25,434 children were born to mothers who had redeemed a beta2AA prescription in pregnancy. The exposed children had a 1.31-fold increased risk [aIRR = 1.30, 95% confidence interval (CI):1.20-1.42] of ADHD compared to unexposed children after adjusting for potential confounders. However, when extending the exposure window to 2 years prior to conception until delivery, exposure to maternal use of beta2AA only before pregnancy, only during pregnancy, and both before and during pregnancy was associated with elevated risks of ADHD in children, with aIRRs of 1.31 (95% CI 1.22-1.40), 1.38 (95% CI 1.22-1.57), and 1.30 (95% CI 1.16-1.45), respectively. In mothers with a history of asthma, no association was observed between maternal use of beta2AA during pregnancy and ADHD in offspring (aIRR = 0.92, 95% CI 0.74-1.15). In utero exposure to beta2AA was associated with an increased risk of ADHD in children. However, it is more likely that confounding by indication, the underlying disorders or associated pathological conditions, may explain the association

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Eur Child Adolesc Psychiatry. 2017 Jun;26:681-89.

PEDIATRIC OBSESSIVE-COMPULSIVE DISORDER WITH TIC SYMPTOMS: CLINICAL PRESENTATION AND TREATMENT OUTCOME.

Hojgaard DRMA, Skarphedinsson G, Nissen JB, et al.

Some studies have shown that children and adolescents with obsessive-compulsive disorder (OCD) and co-morbid tics differ from those without co-morbid tics in terms of several demographic and clinical characteristics. However, not all studies have confirmed these differences. This study examined children and adolescents with OCD and with possible or definite tic specifiers according to the DSM-5 in order to see whether they differ from patients without any tic symptoms regarding clinical presentation and outcome of cognitive behavioral therapy (CBT). The full sample included 269 patients (aged 7-17) with primary DSM-IV OCD who had participated in the Nordic Long-term Treatment Study (NordLOTS). Symptoms of tics were assessed using the Kiddie Schedule for Affective Disorders and Schizophrenia (K-SADS-PL). One or more tic symptoms were found in 29.9% of participants. Those with OCD and co-morbid tic symptoms were more likely male, more likely to have onset of OCD at an earlier age, and differed in terms of OCD symptom presentation. More specifically, such participants also showed more symptoms of OCD-related impairment, externalization, autism spectrum disorder (ASD), social anxiety, and attention-deficit/hyperactivity disorder (ADHD). However, the two groups showed no difference in terms of OCD severity or outcome of CBT. Children and adolescents with OCD and co-morbid tic symptoms differ from those without tic symptoms in several aspects of clinical presentation, but not in their response to CBT. Our results underscore the effectiveness of CBT for tic-related OCD.

CLINICAL TRIALS REGISTRATION: Nordic Long-term Obsessive-Compulsive Disorder (OCD) Treatment Study; www.controlled-trials.com ; ISRCTN66385119

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Eur J Endocrinol. 2017 Nov;177:R261-R273.

MECHANISMS IN ENDOCRINOLOGY: MATERNAL THYROID DYSFUNCTION DURING PREGNANCY AND BEHAVIOURAL AND PSYCHIATRIC DISORDERS OF CHILDREN: A SYSTEMATIC REVIEW.

Fetene DM, Betts KS, Alati R.

BACKGROUND: Maternal thyroid dysfunction during pregnancy may lead to persistent neurodevelopmental disorders in the offspring appearing in later life. This study aimed to review the available evidence concerning the relationship between maternal thyroid status during pregnancy and offspring behavioural and psychiatric disorders.

METHODS: Systematic electronic database searches were conducted using PubMed, Embase, PsycNET, Scopus, Google Scholar and Cochrane library. Studies including gestational thyroid dysfunction as the exposure and offspring behavioural and psychiatric disorders as the outcome were included. The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guideline was followed and, after thorough screening by two independent reviewers, 13 articles remained eligible for inclusion in this study.

RESULTS: Indicators of maternal thyroid dysfunction, including low and high thyroid hormone level and autoimmune thyroiditis, during early pregnancy, were found to be associated with several offspring behavioural and psychiatric disorders such as attention deficit hyperactivity disorder (ADHD), autism, pervasive developmental problems, externalising behaviour, in addition to epilepsy and seizure. The majority of associations were found with low maternal thyroid hormone level.

CONCLUSION: Maternal thyroid function during pregnancy, particularly hypothyroidism, is associated with behavioural and psychiatric disorders in children. Further studies are needed with a capacity to adjust for a fuller range of confounding factors

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Eur Psychiatry. 2017 Jan;39:33-39.

EXPOSURE TO TOBACCO SMOKE IN UTERO OR DURING EARLY CHILDHOOD AND RISK OF HYPOMANIA: PROSPECTIVE BIRTH COHORT STUDY.

Mackay DF, Anderson JJ, Pell JP, et al.

OBJECTIVES: Using data from a prospective birth cohort, we aimed to test for an association between exposure to tobacco smoke in utero or during early development and the experience of hypomania assessed in young adulthood.

METHODS: We used data on 2957 participants from a large birth cohort (Avon longitudinal study of parents and children [ALSPAC]). The primary outcome of interest was hypomania, and the secondary outcome was "hypomania plus previous psychotic experiences (PE)". Maternally-reported smoking during pregnancy, paternal smoking and exposure to environmental tobacco smoke (ETS) in childhood were the exposures of interest. Multivariable logistic regression was used and estimates of association were adjusted for socio-economic, lifestyle and obstetric factors.

RESULTS: There was weak evidence of an association between exposure to maternal smoking in utero and lifetime hypomania. However, there was a strong association of maternal smoking during pregnancy within the sub-group of individuals with hypomania who had also experienced psychotic symptoms (OR=3.45; 95% CI: 1.49-7.98; P=0.004). There was no association between paternal smoking, or exposure to ETS during childhood, and hypomania outcomes.

CONCLUSIONS: Exposure to smoking in utero may be a risk factor for more severe forms of psychopathology on the mood-psychosis spectrum, rather than DSM-defined bipolar disorder

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Eur Child Adolesc Psychiatry. 2018;1-11.

DOES THE EFFICACY OF PARENT' CHILD TRAINING DEPEND ON MATERNAL SYMPTOM IMPROVEMENT? RESULTS FROM A RANDOMIZED CONTROLLED TRIAL ON CHILDREN AND MOTHERS BOTH AFFECTED BY ATTENTION-DEFICIT/HYPERACTIVITY DISORDER (ADHD).

Häge A, Alm B, Banaschewski T, et al.

Multimodal treatment of children with ADHD often includes parent-child training (PCT). However, due to the high heritability, parents of children with ADHD are frequently also affected by the disorder, which is likely to constitute a significant barrier to successful treatment of the child. This secondary analysis of our randomized controlled multicentre AIMAC trial (ADHD in mothers and children) investigates whether children's outcomes following parent-child training in combination with maternal ADHD treatment depend on maternal symptom improvement. In a first step focusing on treatment of maternal ADHD, 144 mothers of mother-child dyads were randomized to multimodal ADHD treatment (group psychotherapy plus methylphenidate) or clinical management (mainly supportive counselling). After 12 weeks (T2), a 12-week PCT program (T2-T3) for all mother-child dyads was added to treat children's ADHD. Maternal symptomatology (CAARS-O:L; SCL-90-R) and children's externalizing symptoms (ADHD-ODD Scale, SDQ) were repeatedly assessed (T1 = baseline, T2, T3). Effects of changes in maternal symptomatology (T1-T2) on the change in children's symptom scores (T1-T3) were analysed using a general linear model, controlling for baseline scores, study centre, and maternal treatment group. 125 mother-child dyads were analysed. Mothers showed significant improvements in ADHD symptoms and overall psychopathology [CAARS-O:L ADHD index: mean - 3.54, SE 0.74 $p < 0.0001$; SCL-90-R Global Severity (GS): mean - 11.03, SE 3.90, $p = 0.0056$]. Although children's externalizing symptoms improved significantly (ADHD-ODD Scale: mean - 4.46, SE 0.58, $p < 0.0001$), maternal improvement had no effect on children's outcomes after Bonferroni-Holm correction for multiple testing. The findings do not support our hypothesis that children's outcomes following PCT for ADHD depend on maternal symptom improvements. Trial register CCT-ISRCTN73911400

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Evid Based Ment Health. 2017 Aug;20:e13.

CHILDHOOD COMORBIDITY AND PARENTAL MENTAL HEALTH PROBLEMS APPEAR TO BE ASSOCIATED WITH ADHD PERSISTENCE.

Agnew-Blais J.

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Horm Res Paediatr. 2018.

THYROID HORMONE STATUS IN OVERWEIGHT CHILDREN WITH ATTENTION DEFICIT/HYPERACTIVITY DISORDER

Langrock C, Hebebrand J, Radowksi K, et al.

BACKGROUND: There is an ongoing discussion whether thyroid hormones are involved in the development and course of attention deficit/hyperactivity disorder (ADHD). Since obesity is associated with both higher thyroid-stimulating hormone (TSH) and free triiodothyronine (fT3) concentrations and increased rates of ADHD, we hypothesized that overweight children with ADHD show higher TSH and fT3 concentrations compared to overweight children without ADHD.

METHODS: TSH, fT3, fT4, and leptin levels were analyzed in 230 children (60.9% boys, 9.3 ± 1.7 years old, 35.7% migration background). The children were divided into four groups (I = 26 overweight children with ADHD, II = 56 normal-weight children with ADHD, III = 66 overweight children without ADHD, and IV = 82 normal-weight children without ADHD). Severity of ADHD was determined by the parent version of the Connors 3® rating scales.

RESULTS: Overweight children with ADHD did not differ significantly from overweight children without ADHD with respect to TSH, fT3, or fT4 concentrations. Comparing the thyroid hormones between the four groups also demonstrated no significant differences for TSH and fT4 concentrations. fT3 concentrations were significantly higher in normal-weight children with ADHD compared to normal-weight children without ADHD. Inattention and hyperactivity/impulsivity scores were not significantly related to TSH or fT3 in multiple regression analyses adjusted for age, gender, and migration background. In these analyses, TSH was

associated with BMI SDS (β coefficient 0.19 ± 0.12, p = 0.002) and leptin (exp[β coefficient] 1.87 ± 1.36, p < 0.001). fT3 (β coefficient 0.06 ± 0.05, p = 0.009) and leptin (exp[β coefficient] 1.17 ± 1.13, p = 0.009) were also associated with BMI SDS.
CONCLUSIONS: Our findings confirm the relation between overweight and thyroid hormones but point against the hypothesis that thyroid hormones might link overweight and ADHD in children

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Hum Mov Sci. 2017 Jun;53:24-36.

THE RELATIONSHIP BETWEEN MOTOR PERFORMANCE AND PARENT-RATED EXECUTIVE FUNCTIONING IN 3- TO 5-YEAR-OLD CHILDREN: WHAT IS THE ROLE OF CONFOUNDING VARIABLES?

Houwen S, van d, V, Visser J, et al.

It is generally agreed that motor performance and executive functioning (EF) are intertwined. As the literature on this issue concerning preschool children is scarce, we examined the relationship between motor performance and parent-rated EF in a sample of 3- to 5-year-old children with different levels of motor skill proficiency, while controlling for age, gender, socio-economic status (SES), and attention-deficit-hyperactivity disorder (ADHD) symptomatology. EF was reported by parents of 153 children (mean age 4years 1months, SD 8months; 75 male) by means of the Behaviour Rating Inventory of Executive Function-Preschool version (BRIEF-P). Parent-reported ADHD symptoms were assessed using the Hyperactivity-Inattention subscale of the Strengths and Difficulties Questionnaire3-4. In addition, the children performed the Movement Assessment Battery for Children-2 (MABC-2). Several weak to moderate relationships were found between the MABC-2 Total Score and the EF subscales. Once other variables such as age, gender, SES, and ADHD symptomatology were taken into account, the only BRIEF-P subscale that was associated with the MABC-2 Total Score was the Working Memory subscale. Compared to their typically developing peers, children who are at risk for motor coordination difficulties (the 16th percentile on the MABC-2) performed poorly on the Working Memory subscale, which confirms the results of the regression analyses. The at risk group also performed significantly worse on the Planning/Organize subscale, however. This is one of the first studies investigating the relationship between motor performance and parent-rated EF in such a young age group. It shows that the relationship between motor performance and EF in young children is complex and may be influenced by the presence of confounding variables such as ADHD symptomatology

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Hum Psychopharmacol. 2017 Mar;32.

DIAGNOSTIC CLUSTERS ASSOCIATED WITH AN EARLY ONSET SCHIZOPHRENIA DIAGNOSIS AMONG CHILDREN AND ADOLESCENTS.

Jerrell JM, McIntyre RS, Deroche CB.

OBJECTIVE: Given the greater severity and chronicity of psychiatric disorders that first declare in individuals under the age of 18, early onset schizophrenia (EOS) and its association with co-occurring psychiatric conditions deserve further investigation.
METHODS: Cluster and discriminant analyses were used to examine the heterogeneity of children and adolescents diagnosed with schizophrenia in 1 statewide system of care. A retrospective cohort design was employed, using South Carolina's (USA) Medicaid claims dataset covering outpatient and inpatient medical services between January, 1999 and December, 2013 to identify patients </=17 years of age.
RESULTS: Among the 613 EOS patients selected, 3 main clusters of ICD-9 psychiatric diagnoses were identified: (1) older children with schizophrenia coaggregated with a spectrum of mood/emotional dysregulation conditions; (2) younger children with coaggregated schizophrenia, mental retardation/intellectual disability or autism spectrum disorders; and (3) older children with schizophrenia and significantly fewer diagnosed co-occurring conditions. Externalizing/disruptive behavior disorders (i.e., attention deficit hyperactivity disorder, conduct disorder, and oppositional defiant disorder) were significantly associated with Clusters 1 and 2.

CONCLUSION: Symptom patterns plus age of first diagnosis are important differentiators of EOS subgroups in this cohort. Earlier recognition of psychiatric symptom/syndrome patterns that frequently co-occur may enable clinicians to stratify/tailor treatment interventions

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Indian J Ophthalmol. 2017 Nov;65:1228-32.

A TINY TICK CAN CAUSE A BIG HEALTH PROBLEM.

John M, Raman M, Ryan K.

Ticks are tiny crawling bugs in the spider family that feed by sucking blood from animals. They are second only to mosquitoes as vectors of human disease, both infectious and toxic. Infected ticks spread over a hundred diseases, some of which are fatal if undetected. They spread the spirochete (which multiplies in the insect's gut) with a subsequent bite to the next host. We describe the only reported cases of peri ocular tick bite from India that presented to us within a span of 3 days and its management. Due suspicion and magnification of the lesions revealed the ticks which otherwise masqueraded as small skin tags/moles on gross examination. The ticks were firmly latched on to the skin and careful removal prevented incarceration of the mouth parts. Rickettsial diseases that were believed to have disappeared from India are reemerging and their presence has recently been documented in at least 11 states in the country. Among vector borne diseases, the most common, Lyme disease, also known as the great mimicker, can present with rheumatoid arthritis, fibromyalgia, depression, attention deficit hyperactivity disorder, multiple sclerosis, chronic fatigue syndrome, cardiac manifestations, encephalitis, and mental illness, to name some of the many associations. Common ocular symptoms and signs include conjunctivitis, keratitis, uveitis, and retinitis. Early detection and treatment of tick borne diseases is important to prevent multi system complications that can develop later in life

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Indian J Physiol Pharmacol. 2017;61:236.

HEART RATE VARIABILITY IN CHILDREN WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER (ADHD) BEFORE AND AFTER TREATMENT WITH METHYLPHENIDATE.

Dogra P, Mondal S, Bandhu R, et al.

Background: Attention-deficit/hyperactivity disorder (ADHD) is one of the most common psychiatric disorders in children and adolescents with estimated worldwide prevalence of 5.29 %. ADHD is associated with autonomic dysfunction which gets further modulated with drug therapy. The heart rate variability (HRV) is validated indicator of the cardiac- autonomic system activity and can be used to study the same in ADHD before and after treatment.

Objectives: There are few prospective studies to evaluate the changes of HRV parameters before and after methylphenidate treatment in drug naive patients with ADHD. Thus the present study was planned with the objective of studying the same among Indian population.

Material and methods: The study approved by IEC for human research included 52 patients of ADHD diagnosed by a psychiatrist were recruited from the Psychiatry OPD of Smt. Sucheta Kriplani Hospital New Delhi. After informed written consent the Baseline ADHD Conners rating score and HRV were recorded. The patients then received methylphenidate therapy. The above parameters were repeated after 12 weeks of study period.

Results: There was a significant improvement (decrease) in the Conners scores. HRV parameters showed a significant increase in the power of Low Frequency component in normalized units (LF nu) and significant decrease in power of high frequency(HF) component in absolute (ms2) as well as normalized units (nu) after methylphenidate treatment. The increase in LF indicates an enhanced sympathetic activity whereas the decrease in HF indicates a decrease in the Parasympathetic activity. The LF: HF ratio showed a significant increase after 12 weeks of MPH treatment indicating shift of sympathovagal balance towards sympathetic dominance. On the Time Domain Parameters the RMSSD decreased significantly after methylphenidate treatment indicating reduced HRV.

Conclusion: The present study shows that with methylphenidate therapy as the ADHD scores improved the autonomic balance shifted in favor of sympathetic preponderance. Moreover reduction in RMSSD indicates reduced HRV and warrants cautious use of methylphenidate in patients vulnerable to cardiac arrhythmias

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Int J Law Psychiatry. 2017 Jan;50:52-60.

A 3-YEAR FOLLOW-UP STUDY OF SWEDISH YOUTHS COMMITTED TO JUVENILE INSTITUTIONS: FREQUENT OCCURRENCE OF CRIMINALITY AND HEALTH CARE USE REGARDLESS OF DRUG ABUSE.

Stahlberg O, Boman S, Robertsson C, et al.

This 3-year follow-up study compares background variables, extent of criminality and criminal recidivism in the form of all court convictions, the use of inpatient care, and number of early deaths in Swedish institutionalized adolescents (N=100) with comorbid substance use disorders (SUD) and Attention-Deficit/Hyperactivity Disorder (ADHD) (n=25) versus those with SUD but no ADHD (n=30), and those without SUD (n=45). In addition it aims to identify whether potential risk factors related to these groups are associated with persistence in violent criminality. Results showed almost no significant differences between the three diagnostic groups, but the SUD plus ADHD group displayed a somewhat more negative outcome with regard to criminality, and the non-SUD group stood out with very few drug related treatment episodes. However, the rate of criminal recidivism was strikingly high in all three groups, and the use of inpatient care as well as the number of untimely deaths recorded in the study population was dramatically increased compared to a age matched general population group. Finally, age at first conviction emerged as the only significant predictor of persistence in violent criminality with an AUC of .69 (CI (95%) .54-.84, p=.02). Regardless of whether SUD, with or without ADHD, is at hand or not, institutionalized adolescents describe a negative course with extensive criminality and frequent episodes of inpatient treatment, and thus requires a more effective treatment than present youth institutions seem to offer today. However, the few differences found between the three groups, do give some support that those with comorbid SUD and ADHD have the worst prognosis with regard to criminality, health, and untimely death, and as such are in need of even more extensive treatment interventions

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Iran J Med Sci. 2018;43:9-17.

EFFECTS OF FOLIC ACID ON APPETITE IN CHILDREN WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER (ADHD) TREATED WITH METHYLPHENIDATE: A RANDOMIZED DOUBLE-BLIND CLINICAL TRIAL.

Riahi F, Tashakori A, Vanani GS.

Background: The highly effective medications in treating attention deficit hyperactivity disorder (ADHD) symptoms are stimulants like methylphenidate. However, they have adverse effects like reduced appetite. We investigated the effects of folic acid on reduced appetite caused by the use of methylphenidate in children with ADHD.

Methods: This randomized double-blind clinical trial evaluated 70 outpatients, aged between 6 and 12 years, with a diagnosis of ADHD. The children were recruited from the Outpatient Child and Adolescent Psychiatric Clinic of Golestan Hospital (Ahwaz, Iran) between 2016 and 2017. The study subjects were randomly assigned to 2 groups: Group 1 received an average dose of methylphenidate (1 mg/kg) plus folic acid (5 mg/d) and Group 2 received an average dose of methylphenidate (1 mg/kg) plus a placebo (5 mg of sucrose) for 8 weeks. Assessments, comprising the Conners Parent Questionnaire, anthropometric measurements, and appetite questionnaire, were conducted by a psychiatrist at baseline and then at 2, 4, 6, and 8 weeks after the medication was started using repeated measure analysis. The data were analyzed with the Mann-Whitney U and ANOVA tests using the SPSS statistical software (v. 18.0).

Results: Age and gender were not associated with the groups. Weight, height, and the body mass index were not changed during the study in both groups. ADHD symptoms significantly decreased in both groups during the trial; however, no difference was observed between the groups. Moreover, appetite was significantly improved in Group 1. Both medications were well tolerated.

Conclusion: It seems that folic acid improved the reduced appetite caused by the use of methylphenidate in our children with ADHD

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J Abnorm Child Psychol. 2017 Jan;45:69-81.

COGNITIVE FUNCTIONING IN ADOLESCENTS WITH SELF-REPORTED ADHD AND DEPRESSION: RESULTS FROM A POPULATION-BASED STUDY.

Roy A, Oldehinkel AJ, Hartman CA.

This study aims to assess cognitive functioning differences among adolescents with retrospectively self-reported: ADHD and an onset of depression, only ADHD, only depression, and neither ADHD nor depression. Data from the Tracking Adolescents' Individual Lives Survey (TRAILS) cohort was used in this study. Neuropsychological functioning was assessed in 1549 adolescents, at baseline and follow-up (mean ages 11 and 19 years). The Composite International Diagnostic Interview was used to classify adolescents into 4 groups: ADHD with onset of depression, only ADHD, only depression, and neither ADHD nor depression. Linear mixed effects models were used to analyse group differences in cognitive functioning at baseline and follow-up, and the change in cognitive functioning between these 2 time-points. Results showed a significant main effect of group on response time variability at baseline, working memory maintenance at follow up, and change in response time variability scores between baseline and follow-up. As compared to the healthy and depressed-only groups, adolescents with only ADHD showed longer response time variability at baseline and, which declined between baseline and follow-up. Adolescents with ADHD plus depression showed higher reaction time for working memory maintenance than the depressed only and healthy groups at follow-up. In conclusion, adolescents with self-reported ADHD show poorer cognitive functioning than healthy adolescents and those with only depression. Amongst adolescents with ADHD, specific cognitive domains show poor functioning depending on the presence or absence of comorbid depression. While adolescents with only ADHD have lower reaction time variability, those with comorbid depression have poorer working memory maintenance

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J Abnorm Child Psychol. 2017 Feb;45:289-300.

THE NATURE OF SOCIAL POSITIVE ILLUSORY BIAS: REFLECTION OF SOCIAL IMPAIRMENT, SELF-PROTECTIVE MOTIVATION, OR POOR EXECUTIVE FUNCTIONING?

McQuade JD, Mendoza SA, Larsen KL, et al.

The present study examined if a social positive illusory bias (PIB) is: a) simply a reflection of low adult-rated social acceptance, b) evident when children's perceived social acceptance is measured implicitly, and c) directly relates to impaired executive functioning (EF). Participants were 8 to 12 year-old children (N = 120; 55 boys and 65 girls) with and without clinical symptoms of attention-deficit/hyperactivity disorder (ADHD). Ratings of the child's social acceptance were obtained from an adult and the child using the Self-Perception Profile for Children (Harter 2012); social bias was calculated as the discrepancy between standardized adult- and child-ratings. Children also completed a reaction time measure to assess implicit perceptions of social acceptance and a battery of EF measures. Depression symptoms were assessed based on parent report. Group comparisons were focused on the presence or absence of social PIB rather than on ADHD diagnostic status. Relative to non-PIB children, those with a social PIB were significantly higher in self-reported social acceptance, but significantly lower on adult reports and implicit perceived social acceptance; these children also were significantly higher in depression symptoms. EF impairments were indirectly related to social PIB as a function of adult-rated social impairment. Results suggest that social PIB is not merely a reflection of low adult-ratings of social acceptance. However, the high explicit self-reports of social acceptance in children with a social PIB are not fully consistent with their implicit self-perceptions of social acceptance. Results are discussed in light of the self-protective and cognitive deficits hypotheses regarding the nature of social PIB

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J Abnorm Child Psychol. 2017 Jan;45:27-43.

THE CHILDREN'S ATTENTION-DEFICIT HYPERACTIVITY DISORDER TELEMENTAL HEALTH TREATMENT STUDY: CAREGIVER OUTCOMES.

Vander SA, McCarty CA, Zhou C, et al.

The Children's Attention-deficit Hyperactivity Disorder (ADHD) Telemental Health Treatment Study (CATTS) tested the hypotheses that children and caregivers who received guideline-based treatment delivered through a hybrid telehealth service delivery model would experience greater improvements in outcomes than children and caregivers receiving treatment via a comparison delivery model. Here, we present caregiver outcomes. 88 primary care providers (PCPs) in seven geographically underserved communities referred 223 children (ages 5.5 - 12.9 years) to the randomized controlled trial. Over 22 weeks, children randomized to the CATTS service delivery model received six sessions of telepsychiatry and six sessions of caregiver behavior management training provided in person by community therapists who were trained and supervised remotely. Children randomized to the comparison Augmented Primary Care (APC) service model received management in primary care augmented by a single telepsychiatry consultation. Caregiver outcomes included changes in distress, as measured by the Patient Health Questionnaire (PHQ-9), Parenting Stress Index (PSI), Caregiver Strain Questionnaire (CSQ) and Family Empowerment Scale (FES). Caregivers completed five assessments. Multilevel mixed effects regression modeling tested for differences between the two service delivery models in caregiver outcomes from baseline to 25 weeks. Compared to caregivers of children in the APC model, caregivers of children in the CATTS service model showed statistically significantly greater improvements on the PHQ-9 (beta = -1.41, 95 % CI = [-2.74, -0.08], p < .05), PSI (beta = -4.59, 95 % CI = [-7.87, - 1.31], p < .001), CSQ (beta = -5.41, 95 % CI = [- 8.58, -2.24], p < .001) and FES (beta = 6.69, 95 % CI = [2.32, 11.06], p < .01). Improvement in child ADHD symptoms mediated improved caregiver scores on the PSI and CSQ. Improvement in child ODD behaviors mediated caregiver CSQ scores. The CATTS trial supports the effectiveness of a hybrid telehealth service delivery model for reducing distress in caregivers of children with ADHD and suggests a mechanism through which the service model affected caregiver distress

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J Abnorm Child Psychol. 2017 Feb;45:273-87.

READING COMPREHENSION IN BOYS WITH ADHD: THE MEDIATING ROLES OF WORKING MEMORY AND ORTHOGRAPHIC CONVERSION.

Friedman LM, Rapport MD, Raiker JS, et al.

Reading comprehension difficulties in children with ADHD are well established; however, limited information exists concerning the cognitive mechanisms that contribute to these difficulties and the extent to which they interact with one another. The current study examines two broad cognitive processes known to be involved in children's reading comprehension abilities-(a) working memory (i.e., central executive processes [CE], phonological short-term memory [PH STM], and visuospatial short-term memory [VS STM]) and (b) orthographic conversion (i.e., conversion of visually presented text to a phonological code)-to elucidate their unique and interactive contribution to ADHD-related reading comprehension differences. Thirty-one boys with ADHD-combined type and 30 typically developing (TD) boys aged 8 to 12 years (M = 9.64, SD = 1.22) were administered multiple counterbalanced tasks assessing WM and orthographic conversion processes. Relative to TD boys, boys with ADHD exhibited significant deficits in PH STM (d = -0.70), VS STM (d = -0.92), CE (d = -1.58), and orthographic conversion (d = -0.93). Bias-corrected, bootstrapped mediation analyses revealed that CE and orthographic conversion processes modeled separately mediated ADHD-related reading comprehension differences partially, whereas PH STM and VS STM did not. CE and orthographic conversion modeled jointly mediated ADHD-related reading comprehension differences fully wherein orthographic conversion's large magnitude influence on reading comprehension occurred indirectly through CE's impact on the orthographic system. The findings suggest that adaptive cognitive interventions designed to improve reading-related outcomes in children with ADHD may benefit by including modules that train CE and orthographic conversion processes independently and interactively

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J Abnorm Child Psychol. 2017 Jan;45:57-68.

USING THE DIFFUSION MODEL TO EXPLAIN COGNITIVE DEFICITS IN ATTENTION DEFICIT HYPERACTIVITY DISORDER.

Huang-Pollock C, Ratcliff R, McKoon G, et al.

Slow, variable, and error-prone performance on speeded reaction time (RT) tasks has been well documented in childhood ADHD, but equally well documented is the context-dependent nature of those deficits, particularly with respect to event rate. As event rates increase (or, as the interstimulus intervals become shorter), RTs decrease, a pattern of performance that has long been interpreted as evidence that cognitive deficits in ADHD are a downstream consequence of a fundamental difficulty in the regulation of arousal to meet task demands. We test the extent to which this is a misinterpretation of the data that occurs when RT and accuracy are considered separately, as is common in neurocognitive research. In two samples of children aged 8-10 with (N = 97; 33 girls) and without (N = 39; 26 girls) ADHD, we used the diffusion model, an influential computational model of RT, to examine the effect of event rate on inhibitory control in a go-no-go task. Contrary to longstanding belief, we found that fast event rates slowed the rate at which children with ADHD accumulated evidence to make a decision to "no-go", as indexed by drift rate. This in turn resulted in a higher proportion of failed inhibits, and occurred despite increased task engagement, as reflected by changes in the starting point of the decision process. Thus, although faster event rates increased task engagement among children with ADHD, the increased engagement was unable to counteract the concurrent slowing of processing speed to "no-go" decisions. Implications for theoretical models of ADHD and treatments are discussed

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J Abnorm Child Psychol. 2017 May;45:719-30.

BEHAVIORAL AND NONDIRECTIVE GUIDED SELF-HELP FOR PARENTS OF CHILDREN WITH EXTERNALIZING BEHAVIOR: MEDIATING MECHANISMS IN A HEAD-TO-HEAD COMPARISON.

Katzmann J, Hautmann C, Greimel L, et al.

Parent training (PT) delivered as a guided self-help intervention may be a cost- and time-effective intervention in the treatment of children with externalizing disorders. In face-to-face PT, parenting strategies have repeatedly been identified as mediating mechanisms for the decrease of children's problem behavior. Few studies have examined possible mediating effects in guided self-help interventions for parents. The present study aimed to investigate possible mediating variables of a behaviorally oriented guided self-help program for parents of children with externalizing problems compared to a nondirective intervention in a clinical sample. A sample of 110 parents of children with externalizing disorders (80 % boys) were randomized to either a behaviorally oriented or a nondirective guided self-help program. Four putative mediating variables were examined simultaneously in a multiple mediation model using structural equation modelling. The outcomes were child symptoms of ADHD and ODD as well as child externalizing problems, assessed at post treatment. Analyses showed a significant indirect effect for dysfunctional parental attributions in favor of the group receiving the behavioral program, and significant effects of the behavioral program on positive and negative parenting and parental self-efficacy, compared to the nondirective intervention. Our results indicate that a decrease of dysfunctional parental attributions leads to a decrease of child externalizing problems when parents take part in a behaviorally oriented guided self-help program. However, none of the putative mediating variables could explain the decrease in child externalizing behavior problems in the nondirective group. A change in dysfunctional parental attributions should be considered as a possible mediator in the context of PT

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J Abnorm Child Psychol. 2017 May;45:777-88.

ATTENTION PROBLEMS AS A MEDIATOR OF THE RELATION BETWEEN EXECUTIVE FUNCTION AND SOCIAL PROBLEMS IN A CHILD AND ADOLESCENT OUTPATIENT SAMPLE.

Hilton DC, Jarrett MA, McDonald KL, et al.

Social functioning is critical for the successful navigation of everyday life for children, adolescents, and adults. Recent theories have postulated a neuropsychological basis for social functioning with particularly strong

links with the executive functioning (EF) system. The current study examined attention problems as a mediator between EF (e.g., working memory, planning, and response inhibition) and social functioning in a child and adolescent outpatient sample. Participants were 218 children ages 6-16 (M = 10.23; SD = 2.52; 68.8 % males) who were referred to an outpatient clinic for psychoeducational assessment. Bias-corrected bootstrapping mediation analyses were used to examine the hypothesized models. The effects of working memory and planning (but not response inhibition) on social problems were mediated by attention problems in both teacher- and mother-reported models. These findings also held up in cross-source models (e.g., mother-reported attention problems as a mediator in a model predicting teacher-reported social problems). These findings have implications for dimensional models of social functioning and conceptual models for specific clinical populations (e.g., attention-deficit/hyperactivity disorder)

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J Abnorm Child Psychol. 2017 May;45:765-76.

CLINICAL, SOCIOBIOLOGICAL, AND COGNITIVE PREDICTORS OF ADHD PERSISTENCE IN CHILDREN FOLLOWED PROSPECTIVELY OVER TIME.

McAuley T, Crosbie J, Charach A, et al.

With increasing awareness that ADHD is chronically disabling, a burgeoning literature has examined childhood clinical indicators of ADHD persistence. This study investigates whether childhood factors reflecting biological risk and cognitive reserve have additive predictive value for the persistence of ADHD that is unique beyond childhood indicators of disorder severity. One-hundred thirty children with ADHD (mean age = 8.9 years, 75 % male) were followed into adolescence (mean age = 14.0 years). Childhood ADHD and co-morbidities were assessed via interviews with parents and teachers; parental psychopathology was assessed via parent interview; exposure to neurobiological and psychosocial adversity were indexed by parent questionnaire; and cognitive reserve was evaluated through children's performance on measures of IQ and executive functioning. Univariate analyses identified childhood inattention and hyperactivity-impulsivity, co-morbid oppositional defiant disorder, overall impairment, and paternal anxiety and depression as more prevalent amongst adolescents with persistent compared with remitted ADHD. Only child-level predictors remained significant in a final multivariate model. These results suggest that children who are most likely to experience persistent ADHD have a more severe clinical presentation in childhood, reflected by increased levels of inattention, oppositional behavior, and impairment. They also are more likely to have fathers with internalizing concerns, but these concerns do not uniquely predict ADHD persistence beyond child-level factors. Contrary to expectations, childhood adversity and cognitive functioning did not predict the course of ADHD

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J Abnorm Child Psychol. 2017 Jan;45:83-90.

IMPULSIVITY SYMPTOMS AS CORE TO THE DEVELOPMENTAL EXTERNALIZING SPECTRUM.

Martel MM, Levinson CA, Lee CA, et al.

Impulsivity is posited to be a key part of the externalizing spectrum during childhood, but this idea has received minimal empirical attention. The goal of the present investigation was to utilize network analysis to determine whether behavioral impulsivity symptoms are key components of the externalizing network across several developmental periods from preschool into adolescence. Participants were 109 preschoolers (64 % male) ages 3 to 6, 237 children (59 % male) ages 6 to 9, 372 children (59 % male) ages 10 to 13, and 357 adolescents (59 % male) ages 13 to 17 and their parents. Parents completed ratings of Attention-Deficit/Hyperactivity Disorder (ADHD) and Oppositional Defiant Disorder (ODD) symptoms on a well-validated rating scale. Network analyses indicated that ADHD and ODD were somewhat differentiated in preschool, becoming united by behavioral impulsivity symptoms during early childhood, and then differentiating into inattention versus externalizing clusters later during childhood and in adolescence. Behavioral impulsivity symptoms were core to the externalizing spectrum across most developmental periods, but core inattentive and ODD symptoms were also identified in line with progressive differentiation. These results suggest the increasing importance of impulsivity symptoms across development, explaining

externalizing comorbidity and potentially serving as a viable target for childhood interventions for externalizing problems

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J Abnorm Child Psychol. 2017 Feb;45:261-72.

NEUROCOGNITIVE PREDICTORS OF ADHD OUTCOME: A 6-YEAR FOLLOW-UP STUDY.

Van LM, Luman M, Twisk JW, et al.

Although a broad array of neurocognitive dysfunctions are associated with ADHD, it is unknown whether these dysfunctions play a role in the course of ADHD symptoms. The present longitudinal study investigated whether neurocognitive functions assessed at study-entry (mean age = 11.5 years, SD = 2.7) predicted ADHD symptom severity and overall functioning 6 years later (mean age = 17.4 years, 82.6 % = male) in a carefully phenotyped large sample of 226 Caucasian participants from 182 families diagnosed with ADHD-combined type. Outcome measures were dimensional measures of ADHD symptom severity and the Kiddie-Global Assessment Scale (K-GAS) for overall functioning. Predictors were derived from component scores for 8 domains of neurocognitive functioning: working memory, motor inhibition, cognitive inhibition, reaction time variability, timing, information processing speed, motor control, intelligence. Effects of age, gender, and pharmacological treatment were considered. Results showed that better working memory predicted lower ADHD symptom severity (R (2) = 3.0 %), and less reaction time variability predicted better overall functioning (higher K-GAS-score, R (2) = 5.6 %). Predictors were still significant with baseline behavior included in the models. The role of neurocognitive functioning in the long term outcome of ADHD behavior is discussed

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J Abnorm Child Psychol. 2017 Feb;45:301-12.

HOW PERSISTENT IS ADHD INTO ADULTHOOD? INFORMANT REPORT AND DIAGNOSTIC THRESHOLDS IN A FEMALE SAMPLE.

Guelzow BT, Loya F, Hinshaw SP.

The persistence of attention-deficit/hyperactivity disorder (ADHD) into adulthood, particularly in women, is an unresolved question. Using a diverse, prospectively followed female sample (ADHD: n = 140; comparison: n = 88), we examined (a) informant (parent- vs. self-report) and (b) symptom threshold (DSM-IV cutoffs vs. a developmentally referenced criterion [DRC]) with respect to estimates of ADHD persistence into young adulthood (M = 19.6 years). We also ascertained the linkages of ADHD status (as measured by each informant and via the different symptom cutoffs) with impairment in key outcome domains. Informant diagnostic concordance was significant but small (kappa = 0.22). Via parent report, more childhood-ascertained probands (44 %) than comparison participants (1 %) met full ADHD criteria in adulthood ($p < 0.001$, varphi = 0.47); parallel results were found via self-report (22 % vs. 2 %; $p < 0.001$, varphi = 0.28). As expected, DRC designations yielded higher persistence estimates than DSM cutoffs. With control of key covariates, parent-reported ADHD was independently associated with poor outcomes on eight of nine measures but self-reported ADHD was associated only with low math scores. Also, participants who met the DRC cutoff but not the higher DSM threshold showed similar impairment to DSM-diagnosed participants, far greater than that of participants who met neither cutoff. A lowered symptom threshold in adulthood compared to childhood appears justified

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J Affect Disord. 2017 Jan;208:198-204.

FACIAL EMOTION LABELING IN UNAFFECTED OFFSPRING OF ADULTS WITH BIPOLAR I DISORDER.

Sharma AN, Barron E, Le CJ, et al.

BACKGROUND: Young people 'at risk' for developing Bipolar Disorder have been shown to have deficits in facial emotion labeling across emotions with some studies reporting deficits for one or more particular emotions. However, these have included a heterogeneous group of young people (siblings of adolescents

and offspring of adults with bipolar disorder), who have themselves diagnosed psychopathology (mood disorders and neurodevelopmental disorders including ADHD).
METHODS: 24 offspring of adults with bipolar I disorder and 34 offspring of healthy controls were administered the Diagnostic Analysis of Non Verbal Accuracy 2 (DANVA 2) to investigate the ability of participants to correctly label 4 emotions: happy, sad, fear and anger using both child and adult faces as stimuli at low and high intensity.
RESULTS: Mixed effects modelling revealed that the offspring of adults with bipolar I disorder made more errors in both the overall recognition of facial emotions and the specific recognition of fear compared with the offspring of healthy controls. Further more errors were made by offspring that were male, younger in age and also in recognition of emotions using 'child' stimuli. LIMITATIONS: The sample size, lack of blinding of the study team and the absence of any stimuli that assess subjects' response to a neutral emotional stimulus are limitations of the study.
CONCLUSIONS: Offspring (with no history of current or past psychopathology or psychotropic medication) of adults with bipolar I disorder displayed facial emotion labeling deficits (particularly fear) suggesting facial emotion labeling may be an endophenotype for bipolar disorder

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J Affect Disord. 2017 Jan;207:175-80.
PREVALENCE AND CORRELATES OF BIPOLAR SPECTRUM DISORDER COMORBID WITH ADHD FEATURES IN NONCLINICAL YOUNG ADULTS.
Wang HR, Jung YE, Chung SK, et al.
BACKGROUND: We investigate the rate of bipolar spectrum disorder comorbid with ADHD features using two screening instruments, the Mood Disorder Questionnaire (MDQ) and the Wender Utah Rating Scale (WURS), in a nonclinical young adult population.
METHODS: College and graduate students aged 18 years or older from four universities in Korea were selected. Comorbidity was defined as both MDQ positivity and WURS positivity. To look for a trend in clinical characteristics according to the severity of the comorbid condition, we used the Jonckheere-Terpstra test and the linear-by-linear association test. We performed ordinal logistic regression analysis to identify predictors associated with the studied comorbid condition.
RESULTS: A total of 1948 subjects were included in the study, and 15 (0.8%) of them were found to have the comorbid condition defined as both MDQ positivity and WURS positivity. As the severity of the comorbid condition increased, we saw trends of lower socioeconomic status, higher history of suicidality, higher history of self-mutilating behavior, higher history of parental abuse or abuse by other people, more severe depression, and more severe problematic alcohol use. The ordinal regression analysis showed that history of parental abuse, depression, and problematic alcohol use predicted the comorbid condition. LIMITATIONS: We did not use standardized diagnostic tools for case findings.
CONCLUSION: The condition of comorbid bipolar spectrum disorder with ADHD features had a notable prevalence of 0.8% in a nonclinical young adult sample. This comorbid condition was found to be related with serious clinical phenomenology

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J Affect Disord. 2017 Jan;208:94-100.
AMYGDALA-PREFRONTAL CORTICAL FUNCTIONAL CONNECTIVITY DURING IMPLICIT EMOTION PROCESSING DIFFERENTIATES YOUTH WITH BIPOLAR SPECTRUM FROM YOUTH WITH EXTERNALIZING DISORDERS.
Hafeman D, Bebko G, Bertocci MA, et al.
OBJECTIVE: Both bipolar spectrum disorders (BPSD) and attention deficit hyperactivity disorder (ADHD) present with emotion-regulation deficits, but require different clinical management. We examined how the neurobiological underpinnings of emotion regulation might differentiate youth with BPSD versus ADHD (and healthy controls, HCs), specifically assessing functional connectivity (FxC) of amygdala-prefrontal circuitry during an implicit emotion processing task.

METHODS: We scanned a subset of the Longitudinal Assessment of Manic Symptoms (LAMS) sample, a clinically recruited cohort with elevated behavioral and emotional dysregulation, and age/sex-ratio matched HCs. Our sample consisted of 22 youth with BPSD, 30 youth with ADHD/no BPSD, and 26 HCs. We used generalized psychophysiological interaction (gPPI) to calculate group differences to emerging emotional faces vs. morphing shapes in FxC between bilateral amygdala and ventral prefrontal cortex/anterior cingulate cortex.
RESULTS: FxC between amygdala and left ventrolateral prefrontal cortex (VLPFC) in response to emotions vs. shapes differed by group (p=.05): while BPSD showed positive FxC (emotions>shapes), HC and ADHD showed inverse FxC (emotions<shapes). A group x emotion interaction was found in amygdala-subgenual cingulate FxC (p=.025), explained by differences in FxC in response to negative emotions. While BPSD showed positive FxC, HC showed inverse FxC; ADHD were intermediate. Amygdala-subgenual FxC was also positively associated with depressive symptoms and stimulant medication.
LIMITATIONS: Co-morbidity and relatively small sample size.
CONCLUSIONS: Youth with BPSD showed abnormally positive FxC between amygdala and regions in the ventral prefrontal cortex during emotion processing. In particular, the amygdala-VLPFC finding was specific to BPSD, and not influenced by other diagnoses or medications

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J Am Acad Child Adolesc Psychiatry. 2017 Mar;56:258-65.
MICROSTRUCTURAL WHITE MATTER ALTERATIONS IN THE CORPUS CALLOSUM OF GIRLS WITH CONDUCT DISORDER.
Menks WM, Furger R, Lenz C, et al.
OBJECTIVE: Diffusion tensor imaging (DTI) studies in adolescent conduct disorder (CD) have demonstrated white matter alterations of tracts connecting functionally distinct fronto-limbic regions, but only in boys or mixed-gender samples. So far, no study has investigated white matter integrity in girls with CD on a whole-brain level. Therefore, our aim was to investigate white matter alterations in adolescent girls with CD.
METHOD: We collected high-resolution DTI data from 24 girls with CD and 20 typically developing control girls using a 3T magnetic resonance imaging system. Fractional anisotropy (FA) and mean diffusivity (MD) were analyzed for whole-brain as well as a priori-defined regions of interest, while controlling for age and intelligence, using a voxel-based analysis and an age-appropriate customized template.
RESULTS: Whole-brain findings revealed white matter alterations (i.e., increased FA) in girls with CD bilaterally within the body of the corpus callosum, expanding toward the right cingulum and left corona radiata. The FA and MD results in a priori-defined regions of interest were more widespread and included changes in the cingulum, corona radiata, fornix, and uncinate fasciculus. These results were not driven by age, intelligence, or attention-deficit/hyperactivity disorder comorbidity.
CONCLUSION: This report provides the first evidence of white matter alterations in female adolescents with CD as indicated through white matter reductions in callosal tracts. This finding enhances current knowledge about the neuropathological basis of female CD. An increased understanding of gender-specific neuronal characteristics in CD may influence diagnosis, early detection, and successful intervention strategies

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J Am Acad Child Adolesc Psychiatry. 2017 Mar;56:234-40.
ASSOCIATIONS BETWEEN AUTOIMMUNE DISEASES AND ATTENTION-DEFICIT/HYPERACTIVITY DISORDER: A NATIONWIDE STUDY.
Nielsen PR, Benros ME, Dalsgaard S.
OBJECTIVE: Recent studies have suggested that autoimmune diseases and immune activation play a part in the pathogenesis of different neurodevelopmental disorders. This study investigated the association between a personal history and a family history of autoimmune disease and the risk of developing attention-deficit/hyperactivity disorder (ADHD).
METHOD: A cohort was formed of all singletons born in Denmark from 1990 to 2007, resulting in a study population of 983,680 individuals followed from 1995 to 2012. Information on autoimmune diseases was

obtained from the Danish National Hospital Register. Individuals with ADHD were identified through the Danish National Hospital Register and the Danish Psychiatric Central Register.
RESULTS: In total, 23,645 children were diagnosed with ADHD during the study period. Autoimmune disease in the individual was associated with an increased risk of ADHD by an incidence rate ratio of 1.24 (95% CI 1.10-1.40). The primary analyses associated maternal autoimmune disease with ADHD in the offspring (incidence rate ratio 1.12, 95% CI 1.06-1.19), whereas a paternal history of autoimmune diseases was not significantly associated with ADHD in the offspring. In exploratory analyses, an increased risk of ADHD was observed for children with a family history of thyrotoxicosis, type 1 diabetes, autoimmune hepatitis, psoriasis, and ankylosing spondylitis.
CONCLUSION: A personal history and a maternal history of autoimmune disease were associated with an increased risk of ADHD. The previously reported association between type 1 diabetes and ADHD was confirmed. In addition, specific parental autoimmune diseases were associated with ADHD in offspring

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J Am Acad Child Adolesc Psychiatry. 2017 Apr;56:286-96.
COGNITIVE IMPAIRMENT IN EUTHYMIC PEDIATRIC BIPOLAR DISORDER: A SYSTEMATIC REVIEW AND META-ANALYSIS.
Elias LR, Miskowiak KW, Vale AM, et al.
OBJECTIVE: To perform a systematic review and meta-analysis of studies investigating neurocognition in euthymic youths with bipolar disorder (BD) compared to healthy controls (HCs).
METHOD: A systematic literature search was conducted in the PubMed/MEDLINE, PsycINFO, and EMBASE databases from inception up until March 23, 2016, for original peer-reviewed articles that investigated neurocognition in euthymic youths with BD compared to HCs. Effect sizes (ES) for individual tests were extracted. In addition, results were grouped according to cognitive domain. This review complied with the PRISMA statement guidelines.
RESULTS: A total of 24 studies met inclusion criteria (N = 1,146; 510 with BD). Overall, euthymic youths with BD were significantly impaired in verbal learning, verbal memory, working memory, visual learning, and visual memory, with moderate to large ESs (Hedge's g 0.76-0.99); significant impairments were not observed for attention/vigilance, reasoning and problem solving, and/or processing speed. Heterogeneity was moderate to large (I(2) >/= 50%) for most ES estimates. Differences in the definition of euthymia across studies explained the heterogeneity in the ES estimate for verbal learning and memory. We also found evidence for other potential sources of heterogeneity in several ES estimates including co-occurring attention-deficit/hyperactivity disorder (ADHD) and anxiety disorders, and the use of medications. In addition, the use of different neuropsychological tests appeared to contribute to heterogeneity of some estimates (e.g., attention/vigilance domain).
CONCLUSION: Euthymic youths with BD exhibit significant cognitive dysfunction encompassing verbal learning and memory, working memory, and/or visual learning and memory domains. These data indicate that for a subset of individuals with BD, neurodevelopmental factors may contribute to cognitive dysfunction

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J Am Acad Child Adolesc Psychiatry. 2017 Mar;56:250-57.
PREDICTORS AND OUTCOMES OF CHILDHOOD PRIMARY ENURESIS.
Kessel EM, Allmann AE, Goldstein BL, et al.
OBJECTIVE: Although enuresis is relatively common in early childhood, research exploring its antecedents and implications is surprisingly limited, perhaps because the condition typically remits in middle childhood.
METHOD: We examined the prevalence, predictors, prognostic factors, and outcomes of primary enuresis in a large (N = 559) multi-method, multi-informant prospective study with a community-based sample of children followed from age 3 years to age 9 years.
RESULTS: We found that 12.7% of our sample met criteria for lifetime enuresis, suggesting that it is a commonly occurring childhood disorder. Males were more than twice as likely as females to have a lifetime diagnosis. Significant age 3 predictors of developing primary enuresis by age 9 included child anxiety and

low positive affectivity, maternal history of anxiety, and low authoritative parenting. In addition, poorer global functioning and more depressive and anxiety symptoms at age 3 years predicted a greater likelihood of persistence through age 9. By age 9 years, 77% of children who had received a diagnosis of primary enuresis were in remission and continent. However, children who had remitted exhibited a higher rate of attention-deficit/hyperactivity disorder (ADHD) and greater ADHD and depressive symptoms at age 9 compared to children with no lifetime history of enuresis.
CONCLUSION: Results of the present study underscore the clinical significance of primary enuresis and demonstrate that it shows both strong antecedent and prospective associations with psychopathology. The findings also highlight the possible role of parenting in the development of enuresis

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J Am Acad Child Adolesc Psychiatry. 2017 Apr;56:304-12.
COURSE OF TOURETTE SYNDROME AND COMORBIDITIES IN A LARGE PROSPECTIVE CLINICAL STUDY.
Groth C, Mol DN, Rask CU, et al.
OBJECTIVE: Tourette syndrome (TS) is a childhood-onset neurodevelopmental disorder characterized by tics and frequent comorbidities. Although tics often improve during adolescence, recent studies suggest that comorbid obsessive-compulsive disorder (OCD) and attention-deficit/hyperactivity disorder (ADHD) tend to persist. This large prospective follow-up study describes the clinical course of tics and comorbidities during adolescence and the prevalence of coexisting psychopathologies.
METHOD: The clinical cohort was recruited at the Danish National Tourette Clinic, and data were collected at baseline (n = 314, age range 5-19 years) and at follow-up 6 years later (n = 227) to establish the persistence and severity of tics and comorbidities. During follow-up, the Development and Well-Being Assessment (DAWBA) was used to diagnose coexisting psychopathologies. Repeated measures of severity scores were modeled using mixed effects models.
RESULTS: Tic severity declined yearly (0.8 points, CI: 0.58-1.01, on the Yale Global Tic Severity Scale [YGTSS]) during adolescence; 17.7% of participants above age 16 years had no tics, whereas 59.5% had minimal or mild tics, and 22.8% had moderate or severe tics. Similarly, significant yearly declines in severity of both OCD (0.24, CI: 0.09-0.39, on the Yale-Brown Obsessive Compulsive Scale for Adults [Y-BOCS] and Yale-Brown Obsessive Compulsive Scale for Children [CY-BOCS]) and ADHD (0.42, CI: 0.32-0.52, DSM-IV) were recorded. At follow-up, 63.0% of participants had comorbidities or coexistent psychopathologies, whereas 37.0% had pure TS.
CONCLUSION: Severity of tics, OCD, and ADHD were significantly associated with age and declined during adolescence. However, considerable comorbidities and coexisting psychopathologies persist throughout adolescence and require monitoring by clinicians

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J Am Acad Child Adolesc Psychiatry. 2017 Jan;56:59-66.
TRENDS IN ANTIPSYCHOTIC PRESCRIBING IN MEDICAID-ELIGIBLE YOUTH.
Edelsohn GA, Karpov I, Parthasarathy M, et al.
OBJECTIVE: To examine trends in the use of antipsychotic medication in Medicaid-eligible youth from 2008 to 2013 and the factors associated with this use.
METHOD: Youth aged 0 to 17 years with at least one claim indicating antipsychotic medication use were identified from the network of a behavioral health managed care organization (BHMCO). Demographic and clinical variables were derived from state eligibility data and service claims data from the BHMCO. Overall and specific prevalence rates of antipsychotic drug use were calculated over the course of 6 years (2008-2013). The probability of antipsychotic use during 2013 was further explored with logistic regression that included demographic and diagnostic groups.
RESULTS: The overall trend in prevalence for antipsychotics for youth decreased from 49.52 per 1,000 members in 2008 to 30.54 in 2013 ($p < .0001$). Although rates decreased for all age groups, the rate per 1,000 members in 2013 for the youngest children was 3.79, versus 39.23 for 6- to 12-year-olds and 64.33 for 13- to 17-year-olds. Controlling for demographic and clinical variables, children 0 to 5 years old were 79%

less likely to be prescribed antipsychotic medications compared to the oldest youth, 13 to 17 years of age (p < .0001). Rates were higher for males versus females regardless of age (odds ratio [95% CI] =1.48 [1.36-1.62], p < .0001). Children with a diagnosis of attention-deficit/hyperactivity disorder were less likely to be prescribed antipsychotics compared to those with diagnoses of autism spectrum disorder, bipolar disorder, psychoses, and depression.
CONCLUSION: Prevalence rates decreased significantly over time for all socio-demographic groups. The largest decrease was observed for the youngest children, ages 0 to 5 years, with a rate in 2013 under half the rate for 2008. Clinical, policy, and managed care implications are discussed

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J Am Acad Child Adolesc Psychiatry. 2017 Mar;56:226-33.
ADOLESCENTS' PRESCRIPTION STIMULANT USE AND ADULT FUNCTIONAL OUTCOMES: A NATIONAL PROSPECTIVE STUDY.
McCabe SE, Veliz P, Wilens TE, et al.
OBJECTIVE: To assess the prospective 17-year relationship between the medical and nonmedical use of prescription stimulants during adolescence (age 18 years) and educational attainment and substance use disorder (SUD) symptoms in adulthood (age 35 years).
METHOD: A survey was self-administered by nationally representative probability samples of US high school seniors from the Monitoring the Future study; 8,362 of these individuals were followed longitudinally from adolescence (age 18, high school senior years 1976-1996) to adulthood (age 35, 1993-2013).
RESULTS: An estimated 8.1% reported medical use of prescription stimulants, and 16.7% reported nonmedical use of prescription stimulants by age 18 years. Approximately 43% of adolescent medical users of prescription stimulants had also engaged in nonmedical use of prescription stimulants during adolescence. Among past-year adolescent nonmedical users of prescription stimulants, 97.3% had used at least one other substance during the past year. Medical users of prescription stimulants without any history of nonmedical use during adolescence did not differ significantly from population controls (i.e., non-attention-deficit/hyperactivity disorder [ADHD] and non-stimulant-medicated ADHD during adolescence) in educational attainment and SUD symptoms in adulthood. In contrast, adolescent nonmedical users of prescription stimulants (with or without medical use) had lower educational attainment and more SUD symptoms in adulthood, compared to population controls and medical users of prescription stimulants without nonmedical use during adolescence.
CONCLUSION: Nonmedical use of prescription stimulants is common among adolescents prescribed these medications. The findings indicate youth should be carefully monitored for nonmedical use because this behavior is associated with lower educational attainment and more SUD symptoms in adulthood

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J Atten Disord. 2017 Jan;21:120-28.
DAILY SYMPTOM PROFILES OF CHILDREN WITH ADHD TREATED WITH MODIFIED-RELEASE METHYLPHENIDATE.
Hautmann C, Rothenberger A, Dopfner M.
OBJECTIVE: The aim was to identify subgroups of patients with ADHD with different daily symptom profiles and to characterize their response to modified-release methylphenidate (MR MPH) treatment, using data from the observational trial OBSEER.
METHOD: OBSEER included patients aged 6 to 17 years receiving MR MPH under routine care. To detect subgroups, a latent class cluster analysis was applied. Sex, age, MR MPH dose, and emotional symptoms were considered predictors of response.
RESULTS: The analysis included 637 patients (81.3% male), with a mean age (standard deviation) of 10.1 (2.5) years. A two-class solution best fit the data, identifying a high-severity group (49.8%) with pronounced symptom reduction, and a low-severity group (50.2%) with minor changes throughout the day. Younger age, male sex, and higher MPH doses were predictive of the high-severity class.

CONCLUSION: Children with ADHD treated with MR MPH are heterogeneous, and subgroups with differential treatment response can be identified

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J Atten Disord. 2017 Jan;21:78-85.

EFFICACY OF POLYUNSATURATED FATTY ACIDS (PUFA) IN THE TREATMENT OF ATTENTION DEFICIT HYPERACTIVITY DISORDER.

Assareh M, Davari AR, Khademi M, et al.

OBJECTIVE: We aimed to investigate the efficacy of polyunsaturated fatty acids (PUFAs) as an adjuvant treatment in patients with ADHD receiving methylphenidate as well as its side effects.

METHOD: This randomized clinical trial was conducted on 40 ADHD patients aged between 6 and 12 years. Both treatment and placebo groups received methylphenidate. Treatment arm also received omega-6 once daily. The Parent ADHD Rating Scale was used to evaluate disease improvement.

RESULTS: The Parent ADHD Rating Scale scores of the two groups were similar at baseline. Although total score and scores of three categories decreased significantly in both groups, total score and scores of inattention, hyperactivity, and impulsivity were not significantly different between the groups.

CONCLUSION: The results did not support the efficacy of PUFA in the treatment of ADHD, and adding PUFAs to the therapeutic regimen of ADHD is not recommended at the moment

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J Atten Disord. 2017 Jan;21:168-79.

CASE SERIES.

Vetrayan J, Othman S, Victor Paulraj SJ.

OBJECTIVE: To assess the effectiveness and feasibility of behavioral sleep intervention for medicated children with ADHD.

METHOD: Six medicated children (five boys, one girl; aged 6-12 years) with ADHD participated in a 4-week sleep intervention program. The main behavioral strategies used were Faded Bedtime With Response Cost (FBRC) and positive reinforcement. Within a case-series design, objective measure (Sleep Disturbance Scale for Children [SDSC]) and subjective measure (sleep diaries) were used to record changes in children's sleep.

RESULTS: For all six children, significant decrease was found in the severity of children's sleep problems (based on SDSC data). Bedtime resistance and mean sleep onset latency were reduced following the 4-week intervention program according to sleep diaries data. Gains were generally maintained at the follow-up. Parents perceived the intervention as being helpful.

CONCLUSION: Based on the initial data, this intervention shows promise as an effective and feasible treatment

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J Atten Disord. 2017 Jan;21:62-70.

DIFFERENTIAL RESPONSE TO METHYLPHENIDATE IN INATTENTIVE AND COMBINED SUBTYPE ADHD .

Beery SH, Quay HC, Pelham WE, Jr.

OBJECTIVE: To examine response to methylphenidate (MPH) assessed by direct observation of ecologically valid behaviors in boys with ADHD with high hyperactivity-impulsivity (HI) and those with predominantly inattentive symptoms (ADHD/I).

METHOD: Sixty-three boys ages 7 to 13 participated in an ADHD Summer Treatment Program and received a double-blind placebo-controlled assessment of .3 mg/kg of MPH on problem behaviors and individualized behavior goals. Medication effect sizes were calculated for each child for each behavior.

RESULTS: Children with ADHD/HI (n = 21) displayed larger MPH effect sizes for interrupting, verbal abuse, and compliance, and marginally greater response for teasing and counselor-directed goals. Children with ADHD/I (n = 21) displayed small medication effect sizes (ds < .20) for many behaviors often identified as

primary deficits in this group (e.g., attention to activities, peer interaction, class work completion, and accuracy).
CONCLUSION: Systematic medication assessment for ADHD/I that quantifies response in ecologically valid areas of functional impairment is essential

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J Atten Disord. 2017 Jun;21:701-11.
SLUGGISH COGNITIVE TEMPO, INTERNALIZING SYMPTOMS, AND EXECUTIVE FUNCTION IN ADULTS WITH ADHD.
Leikauf JE, Solanto MV.
OBJECTIVE: We sought to characterize relationships between sluggish cognitive tempo (SCT) and both internalizing symptoms and executive functioning in adults with ADHD.
METHOD: A total of 102 adults with ADHD completed clinical interviews and clinical rating scales. Hierarchical regression analyses were conducted to ascertain the independent predictive power of SCT symptoms for deficits in executive function (EF) after considering severity of ADHD inattentive and hyperactive-impulsive symptoms and internalizing symptoms.
RESULTS: SCT correlated with ADHD inattentive symptoms and dimensional measures of depression and anxiety but not with clinical diagnosis of depression or anxiety. SCT predicted EF deficits over and above the effects of internalizing and ADHD symptoms. This relationship between SCT and EF was limited to the subset of participants (n = 48) receiving stimulant treatment.
CONCLUSION: SCT in adults with ADHD is associated with internalizing symptoms, ADHD inattentive symptoms, and, independently, with EF deficits. Further research is needed to ascertain why this relationship occurred primarily in adults concurrently receiving stimulants

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J Atten Disord. 2017 Feb;21:240-46.
A PRELIMINARY INVESTIGATION OF THE RELATION BETWEEN THYROID FUNCTIONING AND SLUGGISH COGNITIVE TEMPO IN CHILDREN.
Becker SP, Luebbe AM, Greening L, et al.
OBJECTIVE: To test the hypothesis that thyroid functioning would be uniquely associated with sluggish cognitive tempo (SCT) symptoms but not Diagnostic and Statistical Manual of Mental Disorders (4th ed.; DSM-IV) symptoms of ADHD.
METHOD: Serum thyroid stimulating hormone (TSH) was collected from a sample of psychiatrically hospitalized children (N = 570; ages = 6-12), with rates of TSH similar to those found in the normative pediatric population. Caregivers completed narrowband measures of SCT and ADHD symptoms and broadband measures of internalizing/externalizing symptoms.
RESULTS: A significant, positive relation was found between TSH concentration and SCT symptoms, but not between TSH and ADHD symptoms. Furthermore, regression analyses indicated that the association between TSH and SCT remained significant after controlling for child demographic characteristics, broadband measures of internalizing and externalizing symptoms, and ADHD symptoms. However, effects were small in magnitude.
CONCLUSION: Although preliminary, results indicate that thyroid functioning may be related to SCT. Given the small effects, however, it is important for future research to examine other endocrine and biological correlates that may inform models of the developmental psychopathology of SCT

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J Atten Disord. 2017 Feb;21:219-27.
COMORBIDITY OF ALLERGIC AND AUTOIMMUNE DISEASES AMONG PATIENTS WITH ADHD.
Chen MH, Su TP, Chen YS, et al.

OBJECTIVE: Patients with ADHD have been suggested to have increased risks of allergic diseases but without consistent results, and limited studies about the association between ADHD and autoimmune diseases were noted in the literature.
METHOD: Utilizing the Taiwan National Health Insurance Research Database, ADHD patients were identified and compared with age- and gender-matched controls (1:4).
RESULTS: In all, 8,201 participants were identified as having ADHD, and an increased prevalence of allergic diseases, including asthma (odds ratio [OR] = 1.53), allergic rhinitis (OR = 1.59), atopic dermatitis (OR = 1.53), and urticaria (OR = 1.39), compared with the control group. Although the comorbidity of autoimmune diseases with ADHD was low, ADHD patients had a significantly greater prevalence of ankylosing spondylitis (OR = 2.78), ulcerative colitis (OR = 2.31), and autoimmune thyroid disease (OR = 2.53) than the controls.
CONCLUSION: Our results supported the association between ADHD and allergic/autoimmune diseases. The further studies will be required to clarify the underlying mechanisms

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J Atten Disord. 2017 Jan;21:71-77.
DO STIMULANTS REDUCE THE RISK FOR ALCOHOL AND SUBSTANCE USE IN YOUTH WITH ADHD? A SECONDARY ANALYSIS OF A PROSPECTIVE, 24-MONTH OPEN-LABEL STUDY OF OSMOTIC-RELEASE METHYLPHENIDATE.
Hammerness P, Petty C, Faraone SV, et al.
OBJECTIVE: The purpose of this study was to examine the impact of stimulant treatment on risk for alcohol and illicit drug use in adolescents with ADHD.
METHOD: Analysis of data derived from a prospective open-label treatment study of adolescent ADHD (n = 115, 76% male), and a historical, naturalistic sample of ADHD (n = 44, 68% male) and non-ADHD youth (n = 52, 73% male) of similar age and sex. Treatment consisted of extended-release methylphenidate in the clinical trial or naturalistic stimulant treatment. Self-report of alcohol and drug use was derived from a modified version of the Drug Use Screening Inventory.
RESULTS: Rates of alcohol and drug use in the past year were significantly lower in the clinical trial compared with untreated and treated naturalistic ADHD comparators, and similar to rates in non-ADHD comparators.
CONCLUSION: Well-monitored stimulant treatment may reduce the risk for alcohol and substance use in adolescent ADHD

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J Atten Disord. 2017 Feb;21:343-52.
MEMANTINE IN THE TREATMENT OF EXECUTIVE FUNCTION DEFICITS IN ADULTS WITH ADHD.
Biederman J, Fried R, Tarko L, et al.
OBJECTIVE: To evaluate the efficacy and safety of memantine hydrochloride as an adjunct to stimulant pharmacotherapy for treating executive function deficits (EFDs) in adults with ADHD.
METHOD: This was a 12-week, double-blind, placebo-controlled, randomized clinical trial of memantine added to open-label treatment with stimulant medication. Because of the small sample size, we considered a standardized mean difference (equivalent to effect size) of >/=0.5 and odds ratios >/=2 as indicators of trend improvements.
RESULTS: Twelve participants received memantine and 14 received a placebo. Trend improvements favoring memantine were observed on Behavior Rating Inventory of Executive Functions-Adult Inhibition and Self-Monitor subscales when compared with Placebo. No significant changes were noted on the Cambridge Neuropsychological Test Automated Battery.
CONCLUSION: Among adults with ADHD and EFDs, adjunct treatment with memantine to osmotic release oral system-methylphenidate (OROS-MPH) was associated with improvements in selective areas of executive functioning, supporting the need for further research

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J Atten Disord. 2017 Jun;21:632-41.

SLUGGISH COGNITIVE TEMPO: SOCIODEMOGRAPHIC, BEHAVIORAL, AND CLINICAL CHARACTERISTICS IN A POPULATION OF CATALAN SCHOOL CHILDREN.

Camprodon-Rosanas E, Ribas-Fito N, Batlle-Vila S, et al.

OBJECTIVE: The aims of the present study were to examine the presence of sluggish cognitive tempo (SCT) symptoms in children; associations of the symptoms with sociodemographic characteristics of the children; and relationships between SCT symptoms and symptoms of ADHD, dyslexia, academic performance, and behavioral problems.

METHOD: We evaluated Catalan schoolchildren aged 7 to 10 years in Barcelona, 2012-2013. Parents filled out the SCT-Child Behavior Checklist (SCT-CBCL), the Strengths and Difficulties Questionnaire (SDQ), and a questionnaire concerning sociodemographic characteristics. Teachers completed the ADHD criteria of Diagnostic and Statistical Manual of Mental Disorders (4th ed.; DSM-IV) (

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J Atten Disord. 2017 Jun;21:642-54.

DOES SLUGGISH COGNITIVE TEMPO FIT WITHIN A BI-FACTOR MODEL OF ADHD?

Garner AA, Peugh J, Becker SP, et al.

OBJECTIVE: Studies demonstrate sluggish cognitive tempo (SCT) symptoms to be distinct from inattentive and hyperactive-impulsive dimensions of ADHD. No study has examined SCT within a bi-factor model of ADHD, whereby SCT may form a specific factor distinct from inattention and hyperactivity/impulsivity while still fitting within a general ADHD factor, which was the purpose of the current study.

METHOD: A total of 168 children were recruited from an ADHD clinic. Most (92%) met diagnostic criteria for ADHD. Parents and teachers completed measures of ADHD and SCT.

RESULTS: Although SCT symptoms were strongly associated with inattention, they loaded onto a factor independent of ADHD g. Results were consistent across parent and teacher ratings.

CONCLUSION: SCT is structurally distinct from inattention as well as from the general ADHD latent symptom structure. Findings support a growing body of research suggesting SCT to be distinct and separate from ADHD

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J Atten Disord. 2017 Jan;21:52-61.

ADHD SYMPTOM REBOUND AND EMOTIONAL LABILITY WITH LISDEXAMFETAMINE DIMESYLATE IN CHILDREN Aged 6 TO 12 YEARS.

Lopez FA, Childress A, Adeyi B, et al.

OBJECTIVE: To describe symptom rebound in children with ADHD treated with lisdexamfetamine dimesylate (LDX) or placebo.

METHOD: During a 4-week, randomized, double-blind, placebo-controlled trial of LDX, parents/caregivers completed the Conners' Parent Rating Scale-Revised: Short Form symptom rating scale throughout the day. Response, rebound, and emotional lability (EL) were assessed post hoc based on predefined criteria.

RESULTS: Most participants given LDX (n = 207) were responders throughout the day (50.7%-55.6%) versus placebo (n = 72; 11.1%-22.2%). A total of seven (3.4%) LDX participants showed rebound in the afternoon and/or evening versus seven (9.7%) with placebo. In both groups, most incidences of rebound occurred in the evening. EL (mean) was higher in LDX rebounders and nonresponders (range = 4.2-9.0) versus LDX responders (range = 1.3-1.6) and versus placebo rebounders (range = 0.7-1.9).

CONCLUSION: ADHD symptom rebound occurred in few participants (3.3%) given LDX (accompanied by clinically significant EL). Overall, more participants given LDX versus placebo responded throughout the day

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J Atten Disord. 2017 Jun;21:667-72.

VALIDITY OF SLUGGISH COGNITIVE TEMPO IN SOUTH AMERICA: AN INITIAL EXAMINATION USING MOTHER AND TEACHER RATINGS OF CHILEAN CHILDREN.

Belmar M, Servera M, Becker SP, et al.

OBJECTIVE: To examine the validity of sluggish cognitive tempo (SCT) and ADHD-inattention (ADHD-IN) symptoms in children from Chile.

METHOD: Mothers and teachers rated SCT, ADHD-IN, ADHD-hyperactivity/impulsivity (ADHD-HI), oppositional defiant disorder (ODD), anxiety, depression, academic impairment, social impairment, and peer rejection (teachers only) in 652 Chilean children (55% boys) aged 6 to 14 years.

RESULTS: For both mother and teacher ratings, the eight SCT symptoms and nine ADHD-IN symptoms showed substantial loadings on their respective factors (convergent validity) along with loadings close to zero on the alternative factor (discriminant validity). ADHD-IN showed a uniquely stronger relationship than SCT with ADHD-HI and ODD whereas SCT showed a uniquely stronger relationship than ADHD-IN with anxiety and depression. Although ADHD-IN uniquely predicted academic impairment and social difficulties, SCT did not.

CONCLUSION: This study provides the first evidence for the validity of SCT among children outside of North America or Western Europe

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J Atten Disord. 2017 Jun;21:691-700.

EXECUTIVE DYSFUNCTION AND FUNCTIONAL IMPAIRMENT ASSOCIATED WITH SLUGGISH COGNITIVE TEMPO IN EMERGING ADULTHOOD.

Wood WLM, Lewandowski LJ, Lovett BJ, et al.

OBJECTIVE: Research has identified a relationship between sluggish cognitive tempo (SCT) symptoms and symptoms of ADHD, anxiety, and depression; however, no study has controlled for symptoms of ADHD, anxiety, and depression when examining impairment related to SCT symptoms. This study aimed to examine (a) the extent to which functional impairment and executive function (EF) problems were accounted for by SCT symptoms when controlling for ADHD, anxiety, and depression symptoms, and (b) which type of symptoms were associated with the greatest amount of impairment.

METHOD: College students (N = 458) completed self-report scales of ADHD, SCT, anxiety, and depression symptoms, as well as functional impairment and EF problems.

RESULTS: Thirteen percent of the sample was found to have high levels of SCT symptoms. SCT symptoms showed a moderate to strong correlation with the other symptom sets; however, high levels of SCT symptoms often occurred separate from high levels of ADHD, anxiety, or depression symptoms. SCT symptoms accounted for the most unique variance for both EF problems and functional impairment. Students with high levels of SCT symptoms, with or without high levels of ADHD symptoms, exhibited more impairment and EF problems than the controls.

CONCLUSION: SCT is a clinical construct worthy of additional study, particularly among college students

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J Atten Disord. 2017 Feb;21:247-53.

NEGATIVE AFFECT, DECISION MAKING, AND ATTENTIONAL NETWORKS.

Ortega AR, Ramirez E, Colmenero JM, et al.

This study focuses on whether risk avoidance in decision making depends on negative affect or it is specific to anxious individuals. The Balloon Analogue Risk Task was used to obtain an objective measure in a risk situation with anxious, depressive, and control individuals. The role of attentional networks was also studied using the Attentional Network Test-Interaction (ANT-I) task with neutral stimuli. A significant difference was observed between anxious and depressive individuals in assumed risk in decision making. We found no differences between anxious and normal individuals in the alert, orientation, and congruency effects obtained in the ANT-I task. The results showed that there was no significant relationship between the risk avoidance and the indexes of alertness, orienting, and control. Future research shall determine whether emotionally

relevant stimulation leads to attentional control deficit or whether differences between anxious and no anxious individuals are due to the type of strategy followed in choice tasks

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J Atten Disord. 2017 Mar;21:416-25.

ACCURACY OF ELECTRONIC HEALTH RECORD-DERIVED DATA FOR THE IDENTIFICATION OF INCIDENT ADHD.

Daley MF, Newton DA, Debar L, et al.

OBJECTIVE: To assess the accuracy of electronic health record (EHR)-derived diagnoses in identifying children with incident (i.e., newly diagnosed) ADHD.

METHOD: In 10 large health care organizations, electronic diagnoses data were used to identify all potential cases of incident ADHD among 3- through 9-year-old children. A random sample of records was manually reviewed to determine whether a diagnosis of ADHD was documented in clinician notes.

RESULTS: From electronic diagnoses data, a total of 7,362 children with incident ADHD were identified. Upon manual review of 500 records, the diagnosis of incident ADHD was confirmed in clinician notes for 71.5% (95% confidence interval [CI] = [56.5, 86.4]) of records for 3- through 5-year-old children and 73.6% (95% CI = [65.6, 81.6]) of records for 6- through 9-year-old children.

CONCLUSION: Studies predicated on the identification of incident ADHD cases will need to carefully consider study designs that minimize the likelihood of case misclassification

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J Atten Disord. 2017 Feb;21:305-15.

DEVELOPMENT OF HOT AND COLD EXECUTIVE FUNCTION IN BOYS AND GIRLS WITH ADHD.

Skogli EW, Andersen PN, Hovik KT, et al.

OBJECTIVE: To investigate the development of executive function with pronounced emotional salience (hot EF) and less pronounced emotional salience (cold EF) in boys and girls with ADHD relative to typically developing (TD) children.

METHOD: Seventy-five children with ADHD and 47 TD children were assessed with hot and cold EF tests at baseline and after 2 years.

RESULTS: Despite considerable maturation, the ADHD group remained impaired on all cold EF tests relative to TD children after 2 years. There was no effect of gender on cold EF test results. Females with ADHD outperformed TD counterparts on hot EF at baseline. Females with ADHD showed deteriorating hot EF performance, while TD counterparts showed improved hot EF performance across time.

CONCLUSION: Enduring cold EF impairments after 2 years may reflect stable phenotypic traits in children with ADHD. Results indicate divergent developmental trajectories of hot EF in girls with ADHD relative to TD counterparts

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J Atten Disord. 2017 Feb;21:316-22.

SELF-AWARENESS OF EXECUTIVE FUNCTIONING DEFICITS IN ADOLESCENTS WITH ADHD.

Steward KA, Tan A, Delgaty L, et al.

OBJECTIVE: Children with ADHD lack self-awareness of their social and academic deficits, frequently rating themselves more favorably than external sources. The purpose of the current study was to assess whether adolescents with ADHD also hold a positive bias toward their executive functioning (EF).

METHOD: Participants include 22 control and 35 ADHD subjects, aged 11 to 16. Participants and their parents completed the Behavior Rating Inventory of Executive Functioning (BRIEF) Self and Parent forms, respectively. Discrepancy scores were calculated for each domain by subtracting the adolescents' T-score from the parents' T-score.

RESULTS: Discrepancy scores were significantly higher in the ADHD group than controls within the Inhibit, Shift, Monitor, Emotional Control, Working Memory, and Plan/Organization domains (all $p < .05$).

CONCLUSION: As compared with controls, adolescents with ADHD tend to endorse fewer EF difficulties than what parents report. This is the first study to demonstrate that those with ADHD may overestimate their EF ability

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J Atten Disord. 2017 Feb;21:190-99.

CEREBELLAR SYMPTOMS ARE ASSOCIATED WITH OMISSION ERRORS AND VARIABILITY OF RESPONSE TIME IN CHILDREN WITH ADHD.

Goetz M, Schwabova J, Hlavka Z, et al.

OBJECTIVE: We examined the presence of cerebellar symptoms in ADHD and their association with behavioral markers of this disorder.

METHOD: Sixty-two children with ADHD and 62 typically developing (TD) children were examined for cerebellar symptoms using the ataxia rating scale and tested using Conners' Continuous Performance Test.

RESULTS: Children with ADHD had significantly more cerebellar symptoms compared with the TD children. Cerebellar symptom scores decreased with age in the ADHD group; in the TD group remained stable. In both groups, cerebellar symptoms were associated with parent-rated hyperactive/impulsive symptoms, variability of response time standard error (RT-SE) and increase of RT-SE as the test progresses. More variables were associated with cerebellar symptoms in the ADHD group including omission errors, overall RT-SE and its increase for prolonged interstimulus intervals.

CONCLUSION: Our results highlight the importance of research into motor functions in children with ADHD and indicate a role for cerebellar impairment in this disorder

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J Atten Disord. 2017 Feb;21:284-93.

ARE THERE EXECUTIVE DYSFUNCTION SUBTYPES WITHIN ADHD?

Roberts BA, Martel MM, Nigg JT.

OBJECTIVE: Children with ADHD have heterogeneous behavioral and neuropsychological profiles. The aim of this study was to examine the possible utility of executive function (EF) subtypes within ADHD.

METHOD: Participants were 357 children aged 6 through 13 with a diagnosis of ADHD. Children completed a brief laboratory battery measuring EF, including response inhibition, response variability, speed, and set-shifting. Children also completed standardized intelligence and achievement testing.

RESULTS: Two-way cluster analysis of EF profiles of children with ADHD produced a three-cluster solution, labeled poor inhibitory control, poor set-shifting/speed, and intact task performance. Clusters significantly differed in measures of intelligence, academic achievement, and other disruptive behavior and anxiety/mood symptoms.

CONCLUSION: These findings further support the idea that children with ADHD have heterogeneous EF profiles and suggest that the theory of ADHD should consider these individual differences in EF profiles within the ADHD diagnostic category

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J Atten Disord. 2017 Jan;21:40-45.

THE EFFECTIVENESS OF SHORT- AND LONG-ACTING STIMULANT MEDICATIONS FOR ADOLESCENTS WITH ADHD IN A NATURALISTIC SECONDARY SCHOOL SETTING.

Pelham WE, Smith BH, Evans SW, et al.

OBJECTIVE: Stimulant medication is an efficacious and first-line approach to treating ADHD in adolescence. However, less is known about the effectiveness of this approach as a treatment in real-world settings. The complicated nature of the secondary school environment and documented adolescent nonadherence with stimulant medication may undermine the exportability of this approach.

METHOD: This study investigates stimulant medication effectiveness and adherence in a sample of adolescents with ADHD who were observed in their natural secondary school environment.

RESULTS: Results indicated that the effect of stimulant medication on adolescent functioning is smaller in naturalistic settings than in previous analogue studies. Long-acting pemoline produced greater adherence than the short-acting methylphenidate (MPH), but parents and adolescents preferred the short-acting MPH.
CONCLUSIONS: Overall, adolescents reported very low satisfaction with stimulant medication. Findings are discussed

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J Atten Disord. 2017 Jan;21:158-67.
ACUTE EFFECTS OF MPH ON THE PARENT-TEEN INTERACTIONS OF ADOLESCENTS WITH ADHD.
Pelham WE, Jr., Meichenbaum DL, Smith BH, et al.
This study explored the nature of interactions between adolescent males with ADHD and their mothers, and the effects of methylphenidate (MPH) on an analogue parent-teen interaction task. Twenty-five adolescent males with ADHD (M = 13.6 years) and their mothers and 14 non-ADHD adolescent males (M = 13.4 years) and their mothers completed ratings of perceived dyadic conflict. Behavioral observations of dyads during 10-min conflict-resolution tasks were also collected. The ADHD dyads completed these tasks twice, with adolescents receiving either 0.3 mg/kg MPH or placebo. Videotaped sessions were coded using the Parent-Adolescent Interaction Rating Scale. Following the conflict-resolution task, participants rated their perceived conflict and affect during the interaction. Findings indicated higher conflict in the ADHD dyads, and minimal MPH effects on parent-teen interactions during the analogue task. Results suggest that stimulant medication does not produce meaningful acute effects on parent-teen interactions

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J Atten Disord. 2017 Jun;21:673-83.
ADHD DIMENSIONS AND SLUGGISH COGNITIVE TEMPO SYMPTOMS IN RELATION TO SELF-REPORT AND LABORATORY MEASURES OF NEUROPSYCHOLOGICAL FUNCTIONING IN COLLEGE STUDENTS.
Jarrett MA, Rapport HF, Rondon AT, et al.
OBJECTIVE: This study examined ADHD and sluggish cognitive tempo (SCT) symptoms in relation to self-report and laboratory measures of neuropsychological functioning in college students.
METHOD: College students (N = 298, aged 17-25, 72% female) completed self-reports of ADHD, SCT, depression, sleep, functional impairment, and executive functioning (EF). Participants also completed a visual working memory task, a Stroop test, and the Conners' Continuous Performance Test-II (CPT-II).
RESULTS: ADHD inattentive and SCT symptoms were strong predictors of self-reported EF, with inattention the strongest predictor of Time Management and Motivation and SCT the strongest predictor of Self-Organization/Problem Solving. SCT (but not inattention) was associated with Emotion Regulation. No relationships were found between self-reported symptoms and laboratory task performance. Between-group analyses were largely consistent with regression analyses.
CONCLUSION: Self-reported ADHD and SCT symptoms are strongly associated with college students' self-reported EF, but relationships with laboratory task measures of neuropsychological functioning are limited

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J Atten Disord. 2017 Jun;21:655-66.
EXTERNAL VALIDITY OF ADHD INATTENTION AND SLUGGISH COGNITIVE TEMPO DIMENSIONS IN SPANISH CHILDREN WITH ADHD.
Fenollar CJ, Servera M, Becker SP, et al.
OBJECTIVE: Few studies have examined whether separate dimensions of Sluggish Cognitive Tempo (SCT)-inconsistent alertness and slowness-have different external correlates from each other as well as symptoms of ADHD inattention (ADHD-IN).
METHOD: Participants were 131 Spanish children (ages 6-16; 72% boys) diagnosed with ADHD.
RESULTS: In regression analyses, ADHD-IN was positively associated with hyperactivity/impulsivity, conduct problems, defiance/aggression, anxiety, peer relations problems, and learning problems. SCT-

inconsistent alertness was positively associated with hyperactivity/impulsivity and peer relations problems. In contrast, SCT-slowness was negatively associated with hyperactivity/impulsivity and conduct problems and positively associated with depression and learning problems. Results were consistent after controlling for depression, medication status, and sex.
CONCLUSION: The findings support SCT to be a construct with two dimensions that have unique correlates relative to each other as well as ADHD-IN. Future research on SCT should separate these dimensions of SCT to provide a better understanding of the construct

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J Atten Disord. 2017 Jan;21:149-57.
EFFECTIVENESS AND DURATION OF EFFECT OF OPEN-LABEL LISDEXAMFETAMINE DIMESYLATE IN ADULTS WITH ADHD.
Adler LA, Lynch LR, Shaw DM, et al.
OBJECTIVES: (a) Evaluate the efficacy and duration of effect of lisdexamfetamine dimesylate (LDX) in adult ADHD. (b) Assess the reliability and validity of the Adult ADHD Medication Smoothness of Effect Scale (AMSES) and Adult ADHD Medication Rebound Scale (AMRS).
METHOD: Adults (N = 40) with ADHD were treated with LDX for up to 12 weeks. The primary efficacy measure was the ADHD Rating Scale (ADHD-RS). The psychometric properties of the AMSES and AMRS are analyzed and compared with the ADHD-RS, ADHD Self-Report Scale (ASRS) v1.1 Symptom Checklist, and Time-Sensitive ADHD Symptom Scale (TASS).
RESULTS: ADHD-RS scores were significantly improved with LDX. The AMSES and AMRS had high internal consistency and were correlated with the ADHD-RS, ASRS v1.1 Symptom Checklist, and TASS.
CONCLUSION: LDX is effective in treating adult ADHD and has a smooth drug effect throughout the day with limited symptom rebound. The AMSES and AMRS are valid and reliable measures

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J Atten Disord. 2017 Jan;21:129-36.
ATTRIBUTIONS AND PERCEPTION OF METHYLPHENIDATE EFFECTS IN ADOLESCENTS WITH ADHD.
Pelham WE, Jr., Gnagy EM, Sibley MH, et al.
OBJECTIVE: Although a number of studies demonstrate that children with ADHD do not attribute their behavior to taking medication, it remains unstudied whether adolescents, who have a longer history of taking medication for ADHD, show performance attributions to medication.
METHOD: A sample of 46 adolescents completed daily attributions for success or failure as a part of their participation in a summer treatment program with a double-blind, placebo-controlled assessment of methylphenidate.
RESULTS: Results demonstrated that adolescents with ADHD did not reliably discern active medication from placebo, rarely attributed their performance to the pill, and showed no differences in attributional style as a function of medication status.
CONCLUSION: These data indicate that adolescents with ADHD may possess inaccurate beliefs about the effect of stimulant medication on their behavior

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J Atten Disord. 2017 Feb;21:323-30.
THE RELATIONSHIP BETWEEN EXECUTIVE FUNCTIONS AND QUALITY OF LIFE IN ADULTS WITH ADHD.
Stern A, Pollak Y, Bonne O, et al.
OBJECTIVE: Adult ADHD is associated with impaired quality of life (QoL) and deficient executive function (EF). Given the absence of studies examining the relationship between EF and health-related quality of life (HRQL) in this population, the purpose of the present study was to do so, by the use of rating scales and tests.

METHOD: Adults with ADHD (n = 81) completed ADHD and EF questionnaires and a neuropsychological battery.
RESULTS: Small to large significant correlations were found between EF ratings and HRQL for most of the variables. No significant correlations were found between all but one EF test and HRQL. Both ADHD symptoms and EF rating, but not the EF test, were found to have a unique contribution to the HRQL.
CONCLUSION: These results strengthen the ecological validity of the EF rating scales and their utility in identifying EF deficits with real-world implications for adults with ADHD

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J Atten Disord. 2017 Jun;21:623-31.
CAN SLUGGISH COGNITIVE TEMPO BE DISTINGUISHED FROM ADHD INATTENTION IN VERY YOUNG CHILDREN? EVIDENCE FROM A SAMPLE OF KOREAN PRESCHOOL CHILDREN.
Lee S, Burns GL, Becker SP.
OBJECTIVE: This study evaluated whether sluggish cognitive tempo (SCT) is separable from ADHD-inattention (IN) and uniquely associated with internalizing dimensions in preschool children in South Korea.
METHOD: Mothers of 172 preschool children (ages 4-6 years; 52% girls) rated children's SCT, ADHD-IN, ADHD-hyperactivity/impulsivity (HI), oppositional defiant disorder (ODD), aggression, emotional reactivity, anxiety/depression, somatic complaints, withdrawal, and sleep problems.
RESULTS: Eight of 10 SCT symptoms showed convergent and discriminant validity with ADHD-IN. ADHD-IN remained significantly positively associated with ADHD-HI, ODD, and aggressive behavior after controlling for SCT, whereas SCT was no longer positively associated with these externalizing behaviors after controlling for ADHD-IN. Both SCT and ADHD-IN were uniquely associated with greater emotionally reactivity, anxiety/depression, and withdrawal. Only SCT was uniquely associated with somatic complaints, and only ADHD-IN was uniquely associated with sleep problems.
CONCLUSION: Findings replicate results with children and adolescents, thus expanding evidence for the validity of SCT in early development

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J Atten Disord. 2017 Jan;21:27-39.
AN OPEN-LABEL, RANDOMIZED TRIAL OF METHYLPHENIDATE AND ATOMOXETINE TREATMENT IN ADULTS WITH ADHD.
Ni HC, Lin YJ, Gau SS, et al.
OBJECTIVE: To directly compare the efficacy of methylphenidate and atomoxetine in improving symptoms, social functions, and quality of life among adults with ADHD.
METHOD: This was an 8-to-10-week, open-label, head-to-head, randomized clinical trial with two treatment arms: immediate-release methylphenidate (IR-methylphenidate; n = 31) and atomoxetine once daily (n = 32). The outcome measures included ADHD symptom severity, quality of life, and functional impairments.
RESULTS: We found a significant reduction in overall ADHD symptoms and improvement in social functions and quality of life for both groups at Weeks 4 to 5 and Weeks 8 to 10. There was no significant difference in the slope of improvements over time except that atomoxetine was superior to IR-methylphenidate in reducing hyperactive/impulsive symptoms at Weeks 4 to 5. There was no significant group difference in the rates of adverse effects.
CONCLUSION: Both IR-methylphenidate and atomoxetine are well tolerated and efficacious in ethnic Chinese adults with ADHD

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J Atten Disord. 2017 Feb;21:294-304.

READING PERFORMANCE OF YOUNG ADULTS WITH ADHD DIAGNOSED IN CHILDHOOD.

Miranda A, Mercader J, Fernandez MI, et al.

OBJECTIVE: To study reading performance of young adults with ADHD and its relation with executive functioning.

METHOD: Thirty young adults with a childhood diagnosis of ADHD and 30 with normal development (ND) were compared on reading accuracy, fluency, and comprehension. Furthermore, ADHD with reading disabilities (ADHD+RD) and ADHD without reading disabilities (ADHD-RD) subgroups were compared using self-report and informant-report versions of the Behavior Rating Inventory of Executive Function-Adult version (BRIEF-A).

RESULTS: Adults with ADHD obtained significantly worse results than the ND adults on reading speed, responses to literal questions, and a cloze test. Although the comparison of the ADHD+RD and ADHD-RD groups did not show significant differences on the BRIEF-A subscales, the ADHD+RD group surpassed the critical percentile (85) on more subscales, with working memory and metacognition especially affected.

CONCLUSION: The findings point out that reading should be assessed in individuals with ADHD as part of their evaluation to design effective early interventions

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J Autism Dev Disord. 2017 Mar;47:549-62.

THE COGNITIVE AND BEHAVIORAL PHENOTYPES OF INDIVIDUALS WITH CHRNA7 DUPLICATIONS.

Gillentine MA, Berry LN, Goin-Kochel RP, et al.

Chromosome 15q11q13 is among the least stable regions in the genome due to its highly complex genomic architecture. Low copy repeat elements at 15q13.3 facilitate recurrent copy number variants (CNVs), with deletions established as pathogenic and CHRNA7 implicated as a candidate gene. However, the pathogenicity of duplications of CHRNA7 is unclear, as they are found in affected probands as well as in reportedly healthy parents and unaffected control individuals. We evaluated 18 children with microduplications involving CHRNA7, identified by clinical chromosome microarray analysis (CMA). Comprehensive phenotyping revealed high prevalence of developmental delay/intellectual disability, autism spectrum disorder, and attention deficit/hyperactivity disorder. As CHRNA7 duplications are the most common CNVs identified by clinical CMA, this study provides anticipatory guidance for those involved with care of affected individuals

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J Autism Dev Disord. 2017 Jan;47:155-62.

COMMUNICATION DEFICITS AND THE MOTOR SYSTEM: EXPLORING PATTERNS OF ASSOCIATIONS IN AUTISM SPECTRUM DISORDER (ASD).

Mody M, Shui AM, Nowinski LA, et al.

Many children with autism spectrum disorder (ASD) have notable difficulties in motor, speech and language domains. The connection between motor skills (oral-motor, manual-motor) and speech and language deficits reported in other developmental disorders raises important questions about a potential relationship between motor skills and speech-language deficits in ASD. To this end, we examined data from children with ASD (n = 1781), 2-17 years of age, enrolled in the Autism Speaks-Autism Treatment Network (AS-ATN) registry who completed a multidisciplinary evaluation that included diagnostic, physical, cognitive and behavioral assessments as part of a routine standard of care protocol. After adjusting for age, non-verbal IQ, Attention Deficit Hyperactivity Disorder (ADHD) medication use, and muscle tone, separate multiple linear regression analyses revealed significant positive associations of fine motor skills (FM) with both expressive language (EL) and receptive language (RL) skills in an impaired FM subgroup; in contrast, the impaired gross motor (GM) subgroup showed no association with EL but a significant negative association with RL. Similar analyses between motor skills and interpersonal relationships across the sample found both GM skills and FM skills to be associated with social interactions. These results suggest potential differences in the

contributions of fine versus gross motor skills to autistic profiles and may provide another lens with which to view communication differences across the autism spectrum for use in treatment interventions

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J Autism Dev Disord. 2017 Jan;47:80-89.

INCREASED RISK FOR SUBSTANCE USE-RELATED PROBLEMS IN AUTISM SPECTRUM DISORDERS: A POPULATION-BASED COHORT STUDY.

Butwicka A, Langstrom N, Larsson H, et al.

Despite limited and ambiguous empirical data, substance use-related problems have been assumed to be rare among patients with autism spectrum disorders (ASD). Using Swedish population-based registers we identified 26,986 individuals diagnosed with ASD during 1973-2009, and their 96,557 non-ASD relatives. ASD, without diagnosed comorbidity of attention deficit hyperactivity disorder (ADHD) or intellectual disability, was related to a doubled risk of substance use-related problems. The risk of substance use-related problems was the highest among individuals with ASD and ADHD. Further, risks of substance use-related problems were increased among full siblings of ASD probands, half-siblings and parents. We conclude that ASD is a risk factor for substance use-related problems. The elevated risks among relatives of probands with ASD suggest shared familial (genetic and/or shared environmental) liability

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J Behav Addict. 2017 Dec;6:593-600.

DEVELOPMENT AND VALIDATION OF THE PARENTS' PERCEIVED SELF-EFFICACY TO MANAGE CHILDREN'S INTERNET USE SCALE FOR PARENTS OF ADOLESCENTS WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.

Hsieh YP, Chou WJ, Wang PW, et al.

Background and aims This study developed and validated the Parents' Perceived Self-Efficacy to Manage Children's Internet Use Scale (PSMIS) in the parents of children with attention-deficit/hyperactivity disorder (ADHD).

Methods In total, 231 parents of children with ADHD were invited to complete the PSMIS, followed by the Chen Internet Addiction Scale and the short version of Swanson, Nolan, and Pelham, Version IV Scale - Chinese version for analyzing Internet addiction severity and ADHD symptoms, respectively.

Results The results of exploratory and confirmatory factor analyses confirmed the four-factor structure of the 18-item PSMIS. The significant difference in the levels of parents' perceived self-efficacy between the parents of children with and without Internet addiction supported the criterion-related validity of the PSMIS. The internal consistency and 1-month test-retest reliability were acceptable.

Conclusion The results indicate that the PSMIS has acceptable validity and reliability and can be used for measuring parents' perceived self-efficacy to manage children's Internet use among parents of children with ADHD

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J Child Adolesc Psychiatr Nurs. 2016 Nov;29:188-95.

DECREASING RATES OF PEDIATRIC BIPOLAR WITHIN AN OUTPATIENT PRACTICE.

Wesemann D.

PROBLEM: Pediatric bipolar disorder (PBD) prevalence is estimated to be 1-3%. Nationally and internationally, rates of PBD have increased by over 400%. However, in Iowa and at one psychiatric clinic in Iowa, from 2008-2013, there was a decrease in PBD diagnosis of 33 and 51.2% respectively. This study examined the diagnosing practices of PBD by local providers in one outpatient mental health center.

METHOD: Parents completed a screening packet to differentiate between PBD and attention deficit hyperactivity disorder (ADHD) using three tools: Child Mania Rating Scale (CMRS), Child Behavior Checklist-Mania Scale (CBCL-MS), and the NICHQ Vanderbilt. Symptom agreement analysis between the screeners and the provider's clinical diagnoses was performed using ANOVA and Tukey HSD posthoc analysis.

FINDINGS: A 19.6% of the participants were positive for PBD on the CMRS and 55.9% were positive on the CBCL-MS. A total of 36.60% were positive for ADHD on the Vanderbilt. The screening data compared to the provider's clinical diagnosis showed no diagnostic agreement for PBD ($p < .05$). Providers' rates of diagnosing PBD did not match the rate of PBD symptoms identified by the screeners.
CONCLUSION: Further evidence to determine the criteria and use of current screening measures for PBD is needed to guide practice for distinguishing PBD from related disorders

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J Child Adolesc Psychopharmacol. 2017 Oct;27:678-89.
THE CLINICAL PHARMACOKINETICS OF AMPHETAMINES UTILIZED IN THE TREATMENT OF ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.
Markowitz JS, Patrick KS.
Amphetamine (AMP), an indirectly acting psychostimulant approved for the treatment of attention-deficit/hyperactivity disorder (ADHD) in children, adolescents, and adults, is among the most long-standing therapeutic agents in all of clinical psychopharmacology. This review focuses on AMP absorption, metabolism, and elimination brought to bear on comparative pharmacokinetics in its various formulations. A comprehensive search of the published literature was conducted using MEDLINE (PubMed) and Google Scholar databases through April 2017 to retrieve all pertinent in vitro and human studies for review and synthesis. Additionally, Food and Drug Administration (FDA) databases were accessed for otherwise unavailable data when possible. Initially available as racemic (dl)-AMP, this drug was later supplanted by enantiopure (d)-AMPH or enantioenriched (75:25 dl)-AMP formulations; although racemic AMP returned as an approved drug to treat ADHD in 2014. Presently, there are several immediate-release (IR) formulations available, including d-AMP, dl-AMP, and mixed amphetamine salts, which are neither racemic nor the pure d-enantiomer (i.e., a 3:1 mixture of d-AMP and l-AMP). Furthermore, new modified-release AMP formulations, including an oral suspension and an orally disintegrating tablet, are now available. A lysine-bonded prodrug form of d-AMP also serves as a treatment option. Oral AMP is rapidly absorbed, with high absolute bioavailability, followed by extensive metabolism involving multiple enzymes. Some metabolic pathways exhibit stereoselective biotransformations favoring the l-isomer substrate. Drug exposure exhibits dose-proportional pharmacokinetics. Body weight is a fundamental determinant of differences in observed AMP plasma concentrations. IR formulations typically provide a Tmax from 2 to 3 hours. In replicated studies, children exhibit a shorter plasma T1/2 (
approximately 7 hours) relative to adults (approximately 10 to 12 hours). There are few documented pharmacokinetic drug interactions of clinical significance beyond influences of drug-induced alteration of urinary pH. The array of AMP formulations addressed in this review offer flexibility in dosing, drug onset, and offset to assist in individualized pharmacotherapy of ADHD

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J Child Adolesc Psychopharmacol. 2017 Feb;27:52-65.
THE TREATMENT OF SEVERE CHILDHOOD AGGRESSION STUDY: 12 WEEKS OF EXTENDED, BLINDED TREATMENT IN CLINICAL RESPONDERS.
Findling RL, Townsend L, Brown NV, et al.
OBJECTIVES: Previous "Treatment of Severe Childhood Aggression" (TOSCA) reports demonstrated that many children with severe physical aggression and attention-deficit/hyperactivity disorder (ADHD) responded well to two randomized treatments (parent training [PT]+stimulant+placebo = Basic vs. PT+stimulant+risperidone = Augmented) for 9 weeks. An important clinical question is whether these favorable outcomes are maintained over longer times.
METHODS: Clinical responders to the 9-week trial (n = 103/168), defined as Clinical Global Impressions (CGI)-Improvement of much/very much improved plus substantial reduction in parent ratings of disruptiveness, were followed another 12 weeks (21 weeks total) while remaining on blinded treatment. Outcome measures included Clinical Global Impressions scale, Nisonger Child Behavior Rating Form

(NCBRF), other parent/teacher-rated scales, laboratory tests, clinician ratings of abnormal movement, and other adverse events (AEs).
RESULTS: Parent ratings of problem behavior showed minimal worsening of behavior from end of the 9-week acute trial (expected from regression to the mean after selecting best responders), but outcomes at Extension endpoint were meaningfully improved compared with acute study baseline. As expected, outcomes for Basic and Augmented treatment did not differ among these children selected for good clinical response. During Extension, more Augmented subjects had elevated prolactin; there were no clinically confirmed cases of tardive dyskinesia. Delayed sleep onset was the most frequent Basic AE. We also conducted a last-observation-carried-forward analysis, which included both nonresponders and responders. We found that, at the end of Extension, Augmented subjects had more improvement than Basic subjects on the NCBRF Positive Social subscale ($p = 0.005$; $d = 0.44$), the Antisocial Behavior Scale Reactive Aggression subscale ($p = 0.03$; $d = 0.36$), and marginally so on the Disruptive Behavior Total subscale ($p = 0.058$; $d = 0.29$, the primary outcome).
CONCLUSIONS: The medium-term outcomes were good for the participants in both treatment groups, perhaps because they were selected for good response. When nonresponders were included in ITT analyses, there was some indication that Augmented surpassed Basic treatment

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J Child Adolesc Psychopharmacol. 2017 Oct;27:708-14.
ADVERSE EVENTS OF ATOMOXETINE IN A DOUBLE-BLIND PLACEBO-CONTROLLED STUDY IN CHILDREN WITH AUTISM.
Tumuluru RV, Corbett-Dick P, Aman MG, et al.
OBJECTIVE: Attention-deficit/hyperactivity disorder (ADHD) symptoms, including inattention and over activity, occur in approximately one-third of children with autism spectrum disorder (ASD). We describe the rate and duration of adverse events in a randomized controlled trial of atomoxetine (ATX) and parent training (PT) for ADHD symptoms and noncompliance in children with ASD.
METHODS: We conducted a 10-week, double-blind, 2 x 2 trial of ATX and PT with 128 children (ages 5-14) randomized to ATX alone, ATX+PT, placebo+PT, or placebo alone. For 6 weeks, ATX (or placebo) doses were clinically adjusted to a maximum of 1.8 mg/(kg.day) and maintained for an additional 4 weeks. An average of seven PT sessions were conducted in the two PT arms. Adverse events (AEs) were assessed through parent ratings of common symptoms on a seven-point Likert severity scale and through direct interviews with study medical staff.
RESULTS: ATX was associated with decreased appetite and fatigue, but was otherwise well tolerated. Most reported AEs lasted 4 weeks or less. Unlike reports with typically developing (TD) children, there were no concerns with QTc changes or suicidal ideation.
CONCLUSIONS: This study extends the findings of previous studies of ATX in ASD by documenting that the type of AEs was similar to that of TD children, with no significant safety concerns

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J Child Adolesc Psychopharmacol. 2017 Mar;27:125-31.
USING A PATIENT-CENTERED OUTCOME MEASURE TO TEST METHYLPHENIDATE VERSUS PLACEBO IN CHILDREN WITH AUTISM SPECTRUM DISORDER.
Scahill L, Bearss K, Sarhangian R, et al.
OBJECTIVES: Parent rating scales are commonly used to evaluate change in clinical trials. Despite advantages, these measures may not capture parental impression of the child's most salient problems. We examine the use of parent target problems (PTPs) in a randomized trial of methylphenidate (MPH) in children with autism spectrum disorder and symptoms of attention-deficit/hyperactivity disorder.
METHODS: This multisite, 4-week, randomized crossover trial compared three dose levels (low, medium, and high) of MPH with placebo. At baseline, the independent evaluator (IE) asked parents to nominate the child's two biggest problems. For each problem, the IE and parent coconstructed a brief narrative of the behavior and the impact on family life. The IE and parents reviewed and revised the narratives at subsequent

visits. A panel of four judges, blind to treatment condition, independently reviewed the narratives to rate change from baseline on a 9-point scale: 1, normal; 2, markedly improved; 3, definitely improved; 4, equivocally improved; 5, no change; 6, possibly worse; 7, definitely worse; 8, markedly worse; 9, disastrously worse. The mean of the four raters was compared with primary and key secondary ratings from the original study.
RESULTS: Two PTPs were recorded at baseline for 60 participants. The inter-rater reliability of the four judges across all PTPs and time points was excellent (intraclass correlation = 0.95). On the primary outcome measure (Aberrant Behavior Checklist Hyperactivity subscale), the medium and high-dose levels were superior to placebo. On the mean PTP rating, only the high dose was superior to placebo. We also compared PTP cutoff scores 3.0 (definitely improved), 3.25, and 3.5 with the rate of positive response on the Improvement item of the Clinical Global Impressions scale in the original study. Sensitivities ranged from 68% to 88%.
CONCLUSIONS: The parent target problem method offers a systematic way to identify and track patient-centered outcomes

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J Child Neurol. 2017 Feb;32:215-21.
CEREBELLAR VOLUME IN CHILDREN WITH ATTENTION-DEFICIT HYPERACTIVITY DISORDER (ADHD).
Wyciszkiewicz A, Pawlak MA, Krawiec K.
Attention Deficit Hyperactivity Disorder (ADHD) is associated with altered cerebellar volume and cerebellum is associated with cognitive performance. However there are mixed results regarding the cerebellar volume in young patients with ADHD. To clarify the size and direction of this effect, we conducted the analysis on the large public database of brain images. The aim of this study was to confirm that cerebellar volume in ADHD is smaller than in control subjects in currently the largest publicly available cohort of ADHD subjects. We applied cross-sectional case control study design by comparing 286 ADHD patients (61 female) with age and gender matched control subjects. Volumetric measurements of cerebellum were obtained using automated segmentation with Free Surfer 5.1. Statistical analysis was performed in R-CRAN statistical environment. Patients with ADHD had significantly smaller total cerebellar volumes (134.5+/-17.11cm(3) vs.138.90+/-15.32 cm(3)). The effect was present in both females and males (males 136.9+/-14.37 cm(3) vs. 141.20+/-14.75 cm(3); females 125.7+/-12.34 cm(3) vs. 131.20+/-15.03 cm(3)). Age was positively and significantly associated with the cerebellar volumes. These results indicate either delayed or disrupted cerebellar development possibly contributing to ADHD pathophysiology

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J Child Neurol. 2017 Apr;32:467-74.
PEDIATRIC EPILEPSY SURGERY: THE PROGNOSTIC VALUE OF CENTRAL NERVOUS SYSTEM COMORBIDITIES IN PATIENTS AND THEIR FAMILIES.
Qualmann KJ, Spaeth CG, Myers MF, et al.
Central nervous system comorbidities have been identified in patients with epilepsy. Several of these comorbidities have been correlated with poor surgery outcomes in patient cohorts. The authors sought to determine if prevalence of comorbidities in pediatric epilepsy surgery patients and their families correlate with long-term seizure outcome in a cross-sectional analysis. Three-generation pedigrees were elicited to compare family history of epilepsy, ADHD, anxiety, autism, bipolar disorder, cognitive disability, depression, migraine, and motor disability to surgery outcomes in 52 patients. Proportions of affected patients and relatives were compared to general population comorbidity rates and the patients' most recent seizure outcome classification. Patients and families had significantly higher rates of comorbidities than the general population. Poorer long-term seizure outcomes following resective surgery were associated with autism or cognitive disability in patients. Together these data support evidence for a common pathophysiological mechanism between epilepsy and central nervous system comorbidities

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J Child Psychol Psychiatry. 2017 Jan;58:19-27.
Prenatal unhealthy diet, insulin-like growth factor 2 gene (IGF2) methylation, and attention deficit hyperactivity disorder symptoms in youth with early-onset conduct problems.
Rijlaarsdam J, Cecil CA, Walton E, et al.
BACKGROUND: Conduct problems (CP) and attention deficit hyperactivity disorder (ADHD) are often comorbid and have each been linked to 'unhealthy diet'. Early-life diet also associates with DNA methylation of the insulin-like growth factor 2 gene (IGF2), involved in fetal and neural development. We investigated the degree to which prenatal high-fat and -sugar diet might relate to ADHD symptoms via IGF2 DNA methylation for early-onset persistent (EOP) versus low CP youth.
METHODS: Participants were 164 youth with EOP (n = 83) versus low (n = 81) CP drawn from the Avon Longitudinal Study of Parents and Children. We assessed if the interrelationships between high-fat and -sugar diet (prenatal, postnatal), IGF2 methylation (birth and age 7, collected from blood), and ADHD symptoms (age 7-13) differed for EOP versus low CP youth.
RESULTS: Prenatal 'unhealthy diet' was positively associated with IGF2 methylation at birth for both the EOP and low CP youth. For EOP only: (a) higher IGF2 methylation predicted ADHD symptoms; and (b) prenatal 'unhealthy diet' was associated with higher ADHD symptoms indirectly via higher IGF2 methylation.
CONCLUSIONS: Preventing 'unhealthy diet' in pregnancy might reduce the risk of ADHD symptoms in EOP youth via lower offspring IGF2 methylation

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J Child Psychol Psychiatry. 2017 Apr;58:474-503.
ANNUAL RESEARCH REVIEW: DIGITAL HEALTH INTERVENTIONS FOR CHILDREN AND YOUNG PEOPLE WITH MENTAL HEALTH PROBLEMS - A SYSTEMATIC AND META-REVIEW.
Hollis C, Falconer CJ, Martin JL, et al.
BACKGROUND: Digital health interventions (DHIs), including computer-assisted therapy, smartphone apps and wearable technologies, are heralded as having enormous potential to improve uptake and accessibility, efficiency, clinical effectiveness and personalisation of mental health interventions. It is generally assumed that DHIs will be preferred by children and young people (CYP) given their ubiquitous digital activity. However, it remains uncertain whether: DHIs for CYP are clinically and cost-effective, CYP prefer DHIs to traditional services, DHIs widen access and how they should be evaluated and adopted by mental health services. This review evaluates the evidence-base for DHIs and considers the key research questions and approaches to evaluation and implementation.
METHODS: We conducted a meta-review of scoping, narrative, systematic or meta-analytical reviews investigating the effectiveness of DHIs for mental health problems in CYP. We also updated a systematic review of randomised controlled trials (RCTs) of DHIs for CYP published in the last 3 years.
RESULTS: Twenty-one reviews were included in the meta-review. The findings provide some support for the clinical benefit of DHIs, particularly computerised cognitive behavioural therapy (cCBT), for depression and anxiety in adolescents and young adults. The systematic review identified 30 new RCTs evaluating DHIs for attention deficit/hyperactivity disorder (ADHD), autism, anxiety, depression, psychosis, eating disorders and PTSD. The benefits of DHIs in managing ADHD, autism, psychosis and eating disorders are uncertain, and evidence is lacking regarding the cost-effectiveness of DHIs.
CONCLUSIONS: Key methodological limitations make it difficult to draw definitive conclusions from existing clinical trials of DHIs. Issues include variable uptake and engagement with DHIs, lack of an agreed typology/taxonomy for DHIs, small sample sizes, lack of blinded outcome assessment, combining different comparators, short-term follow-up and poor specification of the level of human support. Research and practice recommendations are presented that address the key research questions and methodological issues for the evaluation and clinical implementation of DHIs for CYP

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J Child Psychol Psychiatry. 2017 Apr;58:439-69.

ANNUAL RESEARCH REVIEW: QUALITY OF LIFE AND CHILDHOOD MENTAL AND BEHAVIOURAL DISORDERS - A CRITICAL REVIEW OF THE RESEARCH.

Jonsson U, Alaie I, Lofgren WA, et al.

BACKGROUND: An individual's subjective perception of well-being is increasingly recognized as an essential complement to clinical symptomatology and functional impairment in children's mental health. Measurement of quality of life (QoL) has the potential to give due weight to the child's perspective.

SCOPE AND METHODOLOGY: Our aim was to critically review the current evidence on how childhood mental disorders affect QoL. First, the major challenges in this research field are outlined. Then we present a systematic review of QoL in children and adolescents aged 0-18 years formally diagnosed with a mental and behavioural disorder, as compared to healthy or typically developing children or children with other health conditions. Finally, we discuss limitations of the current evidence base and future directions based on the results of the systematic review and other relevant literature.

FINDINGS AND CONCLUSIONS: The systematic review identified 41 eligible studies. All were published after the year 2000 and 21 originated in Europe. The majority examined QoL in neurodevelopmental disorders, including attention-deficit hyperactivity disorder (k = 17), autism spectrum disorder (k = 6), motor disorders (k = 5) and intellectual disability (k = 4). Despite substantial heterogeneity, studies demonstrate that self-reported global QoL is significantly reduced compared to typical/healthy controls across several disorders and QoL dimensions. Parents' ratings were on average substantially lower, casting doubt on the validity of proxy-report. Studies for large diagnostic groups such as depressive disorders, anxiety disorders, (early onset) schizophrenia and eating disorders are largely lacking. We conclude that representative, well-characterized normative and clinical samples as well as longitudinal and qualitative designs are needed to further clarify the construct of QoL, to derive measures of high ecological validity, and to examine how QoL fluctuates over time and is attributable to specific conditions or contextual factors

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J Child Psychol Psychiatry. 2017 Jan;58:83-93.

OMEGA 3/6 FATTY ACIDS FOR READING IN CHILDREN: A RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED TRIAL IN 9-YEAR-OLD MAINSTREAM SCHOOLCHILDREN IN SWEDEN .

Johnson M, Fransson G, Ostlund S, et al.

BACKGROUND: Previous research has shown positive effects of Omega 3/6 fatty acids in children with inattention and reading difficulties. We aimed to investigate if Omega 3/6 improved reading ability in mainstream schoolchildren.

METHODS: We performed a 3-month parallel, randomized, double-blind, placebo-controlled trial followed by 3-month active treatment for all subjects. Mainstream schoolchildren aged 9-10 years were randomized 1:1 to receive three Omega 3/6 capsules twice daily or identical placebo. Assessments were made at baseline, 3 months, and 6 months. The primary outcome measure was the Logos test battery for evaluating reading abilities. The trial is registered with ClinicalTrials.gov, number NCT02557477.

RESULTS: The study enrolled 154 children (active n = 78; placebo n = 76), of whom 122 completed the first 3 months (active n = 64; placebo n = 58) and 105 completed the whole study (active/active n = 55; placebo/active n = 50). Outcomes were assessed by per protocol (PP) and intention-to-treat (ITT) analyses. Active treatment was superior to placebo at 3 months for improvement in phonologic decoding time (PP active/placebo difference -0.16; 95% CI -0.03, -0.29; effect size (ES) .44; p = .005; and ITT ES .37; p = .036), in visual analysis time (PP active/placebo difference -0.19; 95% CI -0.05, -0.33; ES .49; p = .013; and ITT ES .40; p = .01), and for boys in phonologic decoding time (PP -0.22; 95% CI -0.03, -0.41; ES .62; p = .004). Children with ADHD-RS scores above the median showed treatment benefits in visual analysis time (PP ES .8, p = .009), reading speed per word (PP ES .61, p = .008), and phonologic decoding time per word (PP ES .85, p = .006). Adverse events were rare and mild, mainly stomach pain/diarrhea (active n = 9, placebo n = 2).

CONCLUSIONS: Compared with placebo, 3 months of Omega 3/6 treatment improved reading ability - specifically the clinically relevant 'phonologic decoding time' and 'visual analysis time' - in mainstream schoolchildren. In particular, children with attention problems showed treatment benefits

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J Child Psychol Psychiatry. 2017 Mar;58:292-304.

EXTERNALIZING PROBLEMS IN CHILDHOOD AND ADOLESCENCE PREDICT SUBSEQUENT EDUCATIONAL ACHIEVEMENT BUT FOR DIFFERENT GENETIC AND ENVIRONMENTAL REASONS.

Lewis GJ, Asbury K, Plomin R.

BACKGROUND: Childhood behavior problems predict subsequent educational achievement; however, little research has examined the etiology of these links using a longitudinal twin design. Moreover, it is unknown whether genetic and environmental innovations provide incremental prediction for educational achievement from childhood to adolescence.

METHODS: We examined genetic and environmental influences on parental ratings of behavior problems across childhood (age 4) and adolescence (ages 12 and 16) as predictors of educational achievement at age 16 using a longitudinal classical twin design.

RESULTS: Shared-environmental influences on anxiety, conduct problems, and peer problems at age 4 predicted educational achievement at age 16. Genetic influences on the externalizing behaviors of conduct problems and hyperactivity at age 4 predicted educational achievement at age 16. Moreover, novel genetic and (to a lesser extent) nonshared-environmental influences acting on conduct problems and hyperactivity emerged at ages 12 and 16, adding to the genetic prediction from age 4.

CONCLUSIONS: These findings demonstrate that genetic and shared-environmental factors underpinning behavior problems in early childhood predict educational achievement in midadolescence. These findings are consistent with the notion that early-childhood behavior problems reflect the initiation of a life-course persistent trajectory with concomitant implications for social attainment. However, we also find evidence that genetic and nonshared-environment innovations acting on behavior problems have implications for subsequent educational achievement, consistent with recent work arguing that adolescence represents a sensitive period for socioaffective development

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J Child Psychol Psychiatry. 2017 Jan;58:75-82.

COMPLEX EFFECTS OF DYSLEXIA RISK FACTORS ACCOUNT FOR ADHD TRAITS: EVIDENCE FROM TWO INDEPENDENT SAMPLES.

Mascheretti S, Trezzi V, Giorda R, et al.

BACKGROUND: Developmental dyslexia (DD) and attention deficit/hyperactivity disorder (ADHD) are among the most common neurodevelopmental disorders, whose etiology involves multiple risk factors. DD and ADHD co-occur in the same individuals much more often than would be expected by chance. Several studies have found significant bivariate heritability, and specific genes associated with either DD or ADHD have been investigated for association in the other disorder. Moreover, there are likely to be gene-by-gene and gene-by-environment interaction effects (G x G and G x E, respectively) underlying the comorbidity between DD and ADHD. We investigated the pleiotropic effects of 19 SNPs spanning five DD genes (DYX1C1, DCDC2, KIAA0319, ROBO1, and GRIN2B) and seven DD environmental factors (smoke, miscarriage, birth weight, breastfeeding, parental age, socioeconomic status, and parental education) for main, either (a) genetic or (b) environmental, (c) G x G, and (d) G x E upon inattention and hyperactivity/impulsivity. We then attempted replication of these findings in an independent twin cohort.

METHODS: Marker-trait association was analyzed by implementing the Quantitative Transmission Disequilibrium Test (QTDT). Environmental associations were tested by partial correlations. G x G were investigated by a general linear model equation and a family-based association test. G x E were analyzed through a general test for G x E in sib pair-based association analysis of quantitative traits.

RESULTS: DCDC2-rs793862 was associated with hyperactivity/impulsivity via G x G (KIAA0319) and G x E (miscarriage). Smoke was significantly correlated with hyperactivity/impulsivity. We replicated the DCDC2 x KIAA0319 interaction upon hyperactivity/impulsivity in the twin cohort.
CONCLUSIONS: DD genetic (DCDC2) and environmental factors (smoke and miscarriage) underlie ADHD traits supporting a potential pleiotropic effect

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J Child Psychol Psychiatry. 2017 Feb;58:151-59.

VARIATION IN COMMON PRESCHOOL SLEEP PROBLEMS AS AN EARLY PREDICTOR FOR DEPRESSION AND ANXIETY SYMPTOM SEVERITY ACROSS TIME.

Whalen DJ, Gilbert KE, Barch DM, et al.

BACKGROUND: Child and adolescent psychopathology has been linked to increased sleep problems, but there has been less investigation of this relationship in younger samples with early-onset psychopathology. This study examined three specific but commonly observed aspects of sleep behaviors in young children - (i) Sleep onset latency, (ii) Refusal to sleep alone, and (iii) Nighttime awakenings - measured during preschool, and investigated whether these sleep problems predicted anxiety and/or depression across the next 6 years until school age (ages 9-13).
METHODS: Data were analyzed from N = 292 participants from a prospective longitudinal study of preschool-age children (ages 3-6). At baseline, parent-reported clinical interviews of psychiatric symptoms, as well as sleep problems were conducted using the Preschool-Age Psychiatric Assessment (PAPA). Follow-up clinical interviews were also conducted annually through school age using the Childhood and Adolescent Psychiatric Assessment (CAPA).
RESULTS: Parent-reported sleep onset latency and refusal to sleep alone were significant independent predictors of MDD and anxiety severity, but not ADHD severity across time, even after controlling for family income-to-needs ratio and maternal internalizing psychopathology. In exploratory analyses using only healthy preschoolers, parent-reported sleep onset latency and refusal to sleep alone also predicted anxiety severity.
CONCLUSIONS: We demonstrate that specific, yet relatively common sleep problems predict diagnostic severity of depression and anxiety across time, but not ADHD. Increased clinical attention to and screening for sleep onset latency and refusal to sleep alone during preschool may be warranted

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J Clin Child Adolesc Psychol. 2017 Jul;46:588-99.

PARENTING STRESS AS A MEDIATOR BETWEEN CHILDHOOD ADHD AND EARLY ADULT FEMALE OUTCOMES.

Gordon CT, Hinshaw SP.

The purpose of this study is to examine the mediating role of parenting stress (both parental distress and stress due to dysfunctional interactions in the mother-daughter relationship [PSDI]) in the link between childhood attention-deficit/hyperactivity disorder (ADHD) status and several important young adult outcomes. The diverse sample comprised 140 girls with ADHD and 88 age- and ethnicity-matched comparisons, evaluated at ages 6-12 years and followed prospectively for five years (M age = 14.2) and 10 years (M age = 19.6). The PSDI experienced by a mother during her daughter's adolescence mediated the link between her daughter's childhood ADHD status and adult externalizing and internalizing symptoms. PSDI also mediated the link between ADHD status and young adult nonsuicidal self-injury and had an indirect effect in the relation between childhood ADHD and young adult depressive symptoms. The mediating role of PSDI with respect to internalizing symptoms and depressive symptoms remained in place even when covarying adolescent internalizing/depressive symptoms. Parenting stress, particularly related to maternal perceptions of dysfunctional interactions with adolescent daughters, serves as a key mediator in the association between

childhood ADHD status and important domains of young adult functioning. Minimizing parenting stress and dysfunctional mother-daughter interactions during adolescence might reduce the risk of adverse adult outcomes for girls with ADHD

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J Clin Psychol. 2017 Jan;73:99-112.

EMOTIONAL DYSREGULATION IN ADULTS WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER-VALIDITY, PREDICTABILITY, SEVERITY, AND COMORBIDITY.

Corbisiero S, Morstedt B, Bitto H, et al.

OBJECTIVES: Attention-deficit/hyperactivity disorder (ADHD) is characterized by inattention, hyperactivity, and impulsivity. However, this triad might not be able to explain the complete spectrum of ADHD symptoms, as emotional dysregulation (ED) frequently seems to accompany the disorder. The aim of this study was to further understand the role of ED in adult ADHD.

METHOD: The sample comprised 393 adults with ADHD without or with comorbidity, and 121 adults without ADHD or any other mental disorder. Additionally, the sample focused on ED. The contribution of core symptoms and the effect of comorbidity on ED were tested and the predictive value of ED for the ADHD diagnosis itself analyzed. Finally, all subjects were categorized into groups-No ADHD, ADHD, and ADHD + ED-to analyze the differences in the severity of ADHD symptomatology in the three groups.

RESULTS: ED levels were found to be elevated in patients with ADHD. The core symptoms affected ED, and the ADHD diagnosis was predicted by ED. The addition of ED to a regression model with the core symptoms was shown to improve the predictability of the ADHD diagnosis. The presence of ED proved to be an indicator of the severity of adult ADHD independent of a present comorbidity.

CONCLUSIONS: ED is a significant symptom in adult patients with ADHD and appears to be associated with ADHD itself. Whilst the presence of other mental disorders intensifies symptoms of ED, ED seems not to manifest solely as a consequence of comorbidity

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J Clin Psychol. 2017 Apr;73:489-99.

ATTENTIONAL CONTROL SCALE FOR CHILDREN: FACTOR STRUCTURE AND CONCURRENT VALIDITY AMONG CHILDREN AND ADOLESCENTS REFERRED FOR ANXIETY DISORDERS.

Melendez R, Bechor M, Rey Y, et al.

OBJECTIVE: The present study examined the factor structure and concurrent validity of the Attentional Control Scale for Children (ACS-C; Muris, de Jong, & Engelen, 2004), a youth self-rating scale of attentional control.

METHOD: A multisource assessment approach was used with 186 children and adolescents referred to an anxiety disorders specialty clinic.

RESULTS: Exploratory factor analysis yielded a 2-factor structure with internally consistent and moderately correlated subscales of Attentional Focusing and Attentional Shifting. Total ACS-C and subscale scores demonstrated significant associations with youth and parent ratings of youth anxiety symptoms, youth self ratings of depressive symptoms, and youth diagnosis of attention deficit-hyperactivity disorder.

CONCLUSIONS: These findings support use of the ACS-C as a self-rating scale of attentional control among referred youth. Future research is encouraged to examine retest reliability of the ACS-C and to evaluate whether its internal structure could be enhanced by removing or modifying items that performed poorly

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J Dev Behav Pediatr. 2017 Feb;38 Suppl 1:S9-S11.

AN 8-YEAR-OLD BIOLOGICAL FEMALE WHO IDENTIFIES HERSELF AS A BOY: PERSPECTIVES IN PRIMARY CARE AND FROM A PARENT.

Kern L, Edmonds P, Perrin EC, et al.

CASE: An 8-year 8-month-old biological female who self-identifies as a boy, Ricardo is brought by his mother for a well-child check to his new pediatrician. Ricardo and his mother report that he is doing well, but have concerns about the upcoming changes associated with puberty. Ricardo states that he is particularly afraid of developing breasts. His mother asks about obtaining a referral to a specialist who can provide "hormone therapy" to delay puberty. Ricardo was adopted from Costa Rica at the age of 2 as a healthy girl named "Angela." From the age of 3, he displayed clear preference for male gender-associated clothes, toys, and games. At age 5, his mother sought care for hyperactivity and sleep problems. He was diagnosed with attention-deficit hyperactivity disorder and sleep onset disorder at age 6, and his symptoms have been well controlled with Adderall and melatonin. Ricardo lives with his parents who are accepting and supportive of his gender preference. He sees a therapist who has experience with gender dysphoria. For the past years, he has attended school as male, with the confidential support of administrators at his elementary school

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J Dev Behav Pediatr. 2017 Jan;38:1-11.

ACADEMIC ACHIEVEMENT IN ADULTS WITH A HISTORY OF CHILDHOOD ATTENTION-DEFICIT/HYPERACTIVITY DISORDER: A POPULATION-BASED PROSPECTIVE STUDY.

Voigt RG, Katusic SK, Colligan RC, et al.

OBJECTIVE: Previous research on the developmental course of attention-deficit/hyperactivity disorder (ADHD) is limited by biased clinic-referred samples and other methodological problems. Thus, questions about adult academic outcomes associated with childhood ADHD remain unanswered. Thus, the objective of this study was to describe academic outcomes in adulthood among incident cases of research-identified childhood ADHD versus non-ADHD referents from a population-based birth cohort.

METHOD: Young adults with research-identified childhood ADHD (N = 232; mean age 27.0 yr; 72.0% men) and referents (N = 335; mean age 28.6 yr; 62.7% men) from a 1976 to 1982 birth cohort (N = 5699) were invited to participate in a followup study and were administered an academic achievement battery consisting of the basic reading component of the Woodcock-Johnson III Tests of Achievement (WJ-III) and the arithmetic subtest of the Wide Range Achievement Test-Third Edition (WRAT-3). Outcomes were compared between the 2 groups using linear regression models, adjusted for age, sex, and comorbid learning disability status.

RESULTS: Childhood ADHD cases scored from 3 to 5 grade equivalents lower on all academic tests compared with referents, with mean (SD) standard scores of 95.7 (8.4) versus 101.8 (8.1) in basic reading; 95.0 (9.3) versus 101.9 (8.5) in letterword identification; 98.2 (8.6) versus 103.2 (9.2) in passage comprehension; 95.7 (9.1) versus 100.9 (9.0) in word attack; and 87.8 (12.9) versus 98.0 (12.0) in arithmetic.

CONCLUSION: This is the first prospective, population-based study of adult academic outcomes of childhood ADHD. Our data provide evidence that childhood onset ADHD is associated with long-term underachievement in reading and math that may negatively impact ultimate educational attainment and occupational functioning in adulthood

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J Dev Behav Pediatr. 2017 Feb;38 Suppl 1:S32-S34.

"WHEN THE PRESCRIPTION PAD IS NOT ENOUGH": ATTENTION-DEFICIT HYPERACTIVITY DISORDER MANAGEMENT 2.0.

Radesky J, Reddy A, Steiner N, et al.

CASE: Jose is a 13-year-old boy who presents to his primary care provider after struggling in school for many years. When he was in the first grade, he was diagnosed at a tertiary center with attention-deficit hyperactivity disorder. Multiple medication trials have produced few benefits and many side effects including poor sleep, morbid thoughts, lack of motivation, and, according to his parents, "he seemed like a robot." He comes now

for his annual physical in April, and the parents tell you that the school is threatening that he be retained in the seventh grade. Parents are very adamant they do not want to try another medication. They have brought you their own and his advisor's Vanderbilt's, which each endorse 7 of 9 inattentive symptoms including trouble organizing, poor attention to detail, and easily distracted and forgetful in daily activities. His birth history and developmental history before beginning formal schooling are unremarkable. His first language was English whereas his parents speak Spanish to each other but not the children. He is healthy and without a history of head trauma, seizures, meningitis, or lead poisoning. An aunt has "learning problems." Jose's family lives in a crowded section of a large urban area. They share an apartment with another family, and both parents are employed full time with his father holding 2 full time jobs working double shifts. Their annual income is at the poverty line. There are 4 children in the family aged between 6 and 13 years. His school has been deemed a "recovery school" because of performing below standard on district-wide achievement tests. His classroom has 27 students, many of whom are English language learners, and he is not on an individualized education plan or 504 accommodations. The family is very concerned about the possibility of retention but have decided that "medicine does not help," and they look to you for other recommendations. Where do you go next?

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J Dev Behav Pediatr. 2017 Feb;38 Suppl 1:S3-S5.

ATTACHED TO A DIAGNOSIS: THE QUANDARY OF SOCIAL DEFICITS AND REACTIVE ATTACHMENT DISORDER.

Phelps R, Eisert D, Schulz S, et al.

CASE: Alex is a 9-year-old boy brought to you, his primary care provider, for a "fifth opinion." You have cared for Alex since he was adopted from a Romanian orphanage at 3 years of age. He has been physically healthy with normal growth parameters and no evidence of fetal alcohol syndrome. Alex has long-standing history of social difficulties, impulsivity, lying, controlling, manipulative behaviors, violent outbursts at home with subsequent lack of remorse, and excessive chatter. You referred Alex to an interdisciplinary child development clinic 2 years ago, where he was diagnosed with reactive attachment disorder (RAD) and attention deficit hyperactivity disorder (ADHD). He was noted to have normal cognitive and language skills. Attachment therapy, stimulant therapy, and school accommodations for ADHD were recommended. Alex received some individual counseling with the school psychologist for a year after the first evaluation, with little improvement in core behaviors. The following year, Alex established care with a psychiatrist and a private counselor. The psychiatrist prescribed a succession of stimulants, each of which worked for only a short time and then had waning effect. The counselor worked with Alex and his parents on managing Alex's behavior, which the family reports has been somewhat helpful. Alex's parents express great frustration and sadness that parenting Alex has been such an ongoing struggle since he was adopted. They note that Alex is superficially friendly, chatty, and charming, with everyone he encounters, including strangers, but he never progresses past such superficial interaction, even with his adoptive parents. The parents express that they are deeply wounded that Alex is not more loving and is not more appreciative of the fact that they rescued him from the orphanage. His parents asked his pediatric clinician about Autism as they observe Alex's lack of real affection and social connection with parents or peers. They also note that Alex has difficulty verbalizing his feelings and that he lies frequently, chatters tangentially, and he can watch the Discovery channel for hours. A neurologist, to whom Alex was referred to evaluate staring spells, reassured the family that the spells did not seem to be epilepsy and also diagnosed Alex with "Asperger's syndrome." The school psychologist, after 2 years of equivocation, recently made Alex eligible for autism spectrum services. During the interview and examination, Alex is funny, friendly, and a bit silly. He uses normal eye contact, seems to enjoy the neuromotor examination, and is eager to show you his cool, new handshake. He engages in easy banter, using normal vernacular and prosody. After the visit, you call the therapist to express your opinion that the RAD diagnosis is valid after all and to ask whether the family is engaged in attachment therapy. The therapist refutes the RAD diagnosis, endorsing Asperger's syndrome (AS) instead and notes that Alex is making good progress in school and in therapy, where he is learning pragmatic skills and basic social skills with the use of social stories. Where do you head next?

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J Dev Behav Pediatr. 2017 Jan;38:12-19.

ASSOCIATION BETWEEN AGE OF BEGINNING PRIMARY SCHOOL AND ATTENTION DEFICIT HYPERACTIVITY DISORDER.

Gokce S, Yazgan Y, Ayaz AB, et al.

OBJECTIVE: In April 2012, the Turkish national education system was modified, and the compulsory school age of entry (first grade) was redefined as a minimum of 60 months and a maximum of 66 months (replacing the former minimum criterion of 72 months). In this study, we hypothesized that students starting school before 72 months (the previous age standard for the first grade) may experience (1) a greater number of symptoms of attention deficit hyperactivity disorder (ADHD) and (2) lower functioning in social, behavioral, and academic domains.

METHOD: We performed a cross-sectional community-based study in the first and second grades of all primary schools (4356 students) located in the Kadikoy county of Istanbul, Turkey. Teachers completed Swanson, Nolan, and Pelham version IV and Conners' Teacher's report forms for symptoms of ADHD, the Perceived Competence Scale for functioning, and a sociodemographic questionnaire.

RESULTS: Among first graders, the group that began primary school before the age of 72 months had a higher ADHD prevalence than both of the groups that began primary school between the ages of 72 to 77 months and 78 to 83 months ($p < .001$ for both groups). ADHD symptoms diminished and academic, social, and behavioral functioning improved with age for the first and second grade students.

CONCLUSION: The probability of displaying ADHD symptoms (and caseness) is greater among the "earlier" beginners, whereas the "conventional" classmates exhibited better academic, social, and behavioral functioning

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J Dev Behav Pediatr. 2017 Feb;38 Suppl 1:S69-S72.

"MEDIA ADDICTION" IN A 10-YEAR-OLD BOY.

Brown S, Scharf MA, Bustos C, et al.

CASE: Bryan is a 10-year-old boy who is brought to his pediatrician by his parents with concerns about oppositional behaviors. Bryan's parents report that he has always been hyperactive and oppositional since a very young age. He has been previously diagnosed with attention-deficit hyperactivity disorder and has been treated with appropriate stimulant medications for several years; however, despite this, his parents feel increasingly unable to manage his difficult behaviors. He refuses to do chores or follow through with household routines. He refuses to go to bed at night. His family feels unable to take him to public places because he "climbs all over everything." At school, he acts up in class, is often disruptive, and requires close supervision by teachers. He was recently kicked off of the school bus. He has very few friends, and his parents state that other children do not enjoy to be around him. Bryan's parents also report that he is "obsessed" with electronics. He spends most his free time watching TV and movies and playing computer games. He has a television in his bedroom because otherwise he "monopolizes" the family television. The family also owns several portable electronic devices that he frequently uses. Bryan insists on watching TV during meals and even that the TV stays on in an adjacent room while showering. He gets up early each morning and turns on the television. He refuses to leave the house unless he can take a portable screen device with him. His parents admit to difficulty placing limits on this behavior because they feel it is the only way to keep his other behaviors under control. His mother explains "it is our only pacifier" and that attempts to place restrictions are met with explosive tantrums and have thus been short lived. These efforts have also been impeded due to the habits of his parents and older sibling, who also enjoy spending a significant amount of time watching television

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J Dev Behav Pediatr. 2017 Jan;38:20-28.

IMPACT OF MENTAL HEALTH COMORBIDITIES ON THE COMMUNITY-BASED PEDIATRIC TREATMENT AND OUTCOMES OF CHILDREN WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER.

Al GN, Langberg JM, Gardner W, et al.

OBJECTIVE: Children with attention deficit hyperactivity disorder (ADHD) often exhibit psychiatric comorbidities, which may impact illness presentation, diagnosis, and treatment outcomes. Guidelines exist for dealing with these complex cases but little is known about how comorbidities are being handled in community pediatric settings. The purpose of this study was to evaluate how mental health comorbidities affect community physicians' ADHD care practices and patients' symptom trajectories.

METHOD: Medical charts of 319 children presenting at primary care clinics for ADHD-related concerns were reviewed. Physician assessment and treatment behaviors were extracted and parents rated ADHD symptoms at the time of diagnosis and at 3, 6, and 12 months. Baseline ratings were used to group children, as no comorbid mental health condition, internalizing, or externalizing comorbid condition. Multilevel analyses compared community physician care behaviors and ADHD symptom trajectories across groups.

RESULTS: Approximately, 50 percent of the sample met screening criteria for a comorbid mental health condition. For children diagnosed with ADHD and treated with medication, community physician care largely did not differ across groups, but children with internalizing comorbidities made significantly smaller improvements in inattentive and hyperactive/impulsive symptoms compared with children with no comorbidities.

CONCLUSION: Children with ADHD and mental health comorbidities, particularly internalizing disorders, exhibit less robust response to ADHD medication and may require additional testing before starting medication and/or alternative treatment approaches. Potential barriers to conducting comprehensive assessments and to providing multi-modal treatment are discussed

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J Dev Behav Pediatr. 2017 Feb;38 Suppl 1:S44-S46.

"MORE THAN MEETS THE EYE": WHEN THE NEONATAL COURSE MAY IMPACT SEVERAL YEARS OUT.

Dopwell F, Maypole J, Sinha B, et al.

CASE: Nadia is a 7-year-old girl who you have followed since her discharge from the Neonatal Intensive Care Unit (NICU). Her parents are here today for an urgent visit with behavioral concerns, such as inattention, hyperactivity, and aggression.Nadia is a former 40-weeker born through vacuum-assisted vaginal delivery at 9 pounds 7 ounces. Her delivery was complicated with shoulder dystocia, which resulted in resuscitation. Her Apgar scores were 1, 3, and 4 at 1, 5, and 10 minutes, respectively. After intubation and stabilization on mechanical ventilation, Nadia was transferred to the NICU. Her neonatal course included systemic hypothermia using "cool cap" for hypoxic-ischemic encephalopathy (HIE) for a duration of 72 hours. She was extubated on day of life 3. She had an occupational therapy consultation for poor suck/feeding, and it quickly improved. She was discharged on day of life 14. On discharge, Nadia was referred to early intervention (EI) and the NICU follow-up clinic. Nadia was followed by EI until 12 months of age and in the NICU follow-up clinic until 18 months of age, as there were no concerns meeting her developmental milestones or her neuromotor development.At this urgent visit, Nadia's parents report that she attended a family child care from 1.5 to 3 years of age, Head Start from 3 to 5 years of age and the local public school from 5 years to present. Since starting child care, Nadia's teachers have reported that she requires a lot of redirection and refocusing, fidgets a lot in class, and can be aggressive toward her peers when unprovoked. Since her parents had not seen these behaviors at home, they thought it was a phase that she would grow out of. However, as they began to work with her to complete school assignments, they noticed that it was very difficult for Nadia to sit still and focus on work. They also struggled in the mornings to get her ready and off to school.The parents bring in Conners scales completed by themselves and her lead teacher, and with these and our clinical observations, we diagnose her with attention-deficit/hyperactivity disorder (ADHD), combined type. We

discuss risk factors and ADHD management with her parents. During our discussion, Nadia's father, who has done some reading on ADHD, remembers reading an article about HIE and NICU stay being risk factors for ADHD. He wonders if this affects the choice of management of her ADHD symptoms. How would you address his query?

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J Gambl Stud. 2017 Jun;33:449-60.

DO HIGH SCHOOL STUDENTS IN INDIA GAMBLE? A STUDY OF PROBLEM GAMBLING AND ITS CORRELATES.

Jaisoorya TS, Beena KV, Beena M, et al.

Studies from the West suggest that significant numbers of high school students gamble, despite it being illegal in this age group. To date, there have been no studies on the prevalence of gambling among senior high school and higher secondary school students in India. This study reports point prevalence of gambling and its psychosocial correlates among high school students in the State of Kerala, India. 5043 high school students in the age group 15-19 years, from 73 schools, were selected by cluster random sampling from the district of Ernakulam, Kerala, South India. They completed questionnaires that assessed gambling, substance use, psychological distress, suicidality, and symptoms of Attention Deficit Hyperactivity Disorder (ADHD). Of a total of 4989 completed questionnaires, 1400 (27.9 %) high school students reported to have ever gambled and 353 (7.1 %) were problem gamblers. Of those who had ever gambled, 25.2 % were problem gamblers. Sports betting (betting on cricket and football) was the most popular form of gambling followed by the lottery. Problem gamblers when compared with non-problem gamblers and non-gamblers were significantly more likely to be male, have academic failures, have higher rates of lifetime alcohol and tobacco use, psychological distress, suicidality, history of sexual abuse and higher ADHD symptom scores. Gambling among adolescents in India deserves greater attention, as one in four students who ever gambled was a problem gambler and because of its association with a range of psychosocial variables

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J Learn Disabil. 2017 Mar;50:115-27.

IMPACT OF INTENSIVE SUMMER READING INTERVENTION FOR CHILDREN WITH READING DISABILITIES AND DIFFICULTIES IN EARLY ELEMENTARY SCHOOL.

***Christodoulou JA, Cyr A, Murtagh J, et al*.**

Efficacy of an intensive reading intervention implemented during the nonacademic summer was evaluated in children with reading disabilities or difficulties (RD). Students (ages 6-9) were randomly assigned to receive Lindamood-Bell's Seeing Stars program (n = 23) as an intervention or to a waiting-list control group (n = 24). Analysis of pre- and posttesting revealed significant interactions in favor of the intervention group for untimed word and pseudoword reading, timed pseudoword reading, oral reading fluency, and symbol imagery. The interactions mostly reflected (a) significant declines in the nonintervention group from pre- to posttesting, and (2) no decline in the intervention group. The current study offers direct evidence for widening differences in reading abilities between students with RD who do and do not receive intensive summer reading instruction. Intervention implications for RD children are discussed, especially in relation to the relevance of summer intervention to prevent further decline in struggling early readers

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J Med Syst. 2017 Jul;41:111.

DUAL SYSTEM FOR ENHANCING COGNITIVE ABILITIES OF CHILDREN WITH ADHD USING LEAP MOTION AND EYE-TRACKING TECHNOLOGIES.

***Garcia-Zapirain B, de la TD, I, Lopez-Coronado M*.**

Attention Deficit Hyperactivity Disorder (ADHD) is a brain disorder marked by an ongoing pattern of inattention and/or hyperactivity-impulsivity that affects with development or functioning. It affects 3-5% of all American and European children. The objective of this paper is to develop and test a dual system for the rehabilitation of cognitive functions in children with ADHD. A technological platform has been developed

using the ". NET framework", which makes use of two physiological sensors, -an eye-tracker and a hand gesture recognition sensor- in order to provide children with the opportunity to develop their learning and attention skills. The two physiological sensors we utilized for the development are the Tobii X1 Light Eye Tracker and the Leap Motion. SUS and QUIS questionnaires have been carried out. 19 users tested the system and the average age was 10.88 years (SD = 3.14). The results obtained after tests were performed were quite positive and hopeful. The learning of the users caused by the system and the interfaces item got a high punctuation with a mean of 7.34 (SD = 1.06) for SUS questionnaire and 7.73 (SD = 0.6) for QUIS questionnaire. We didn't find differences between boys and girls. The developed multimodal rehabilitation system can help to children with attention deficit and learning issues. Moreover, the teachers may utilize this system to track the progression of their students and see their behavior

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J Neurotrauma. 2017 Jan;34:322-27.

CONSISTENCY OF SELF-REPORTED CONCUSSION HISTORY IN ADOLESCENT ATHLETES.

Wojtowicz M, Iverson GL, Silverberg ND, et al.

Relying on self-reported concussion injury history is common in both clinical care and research. However, young athletes may not provide consistent medical information. To date, little is known about the reliability of self-reported concussion history in high school students. This study examined whether student athletes reported their lifetime history of concussions consistently over time. Self-reported concussion history was examined in 4792 student athletes (ages 13-18) from Maine who completed a preseason health survey on two occasions (median re-test interval = 23.7 months; standard deviation = 7.3; interquartile range = 12.4-24.5). Consistency of self-reported concussion history was determined by differences in the number of concussions reported during the second survey. Inconsistent concussion history was defined primarily by a decrease in the number of lifetime concussions reported at the second testing, compared with at the first testing. The majority of the sample (80.3%) reported no change in the number of concussions between the two baseline assessments. A minority (15.9%; n = 763) reported more concussions during the second assessment. Only 3.8% (n = 181) of student athletes provided inconsistent concussion histories, defined as fewer concussions at the second assessment. Boys provided inconsistent concussion histories a little more frequently, compared with girls (5.3% and 2.0%, respectively; $p < 0.001$). Similarly, athletes with self-reported attention-deficit hyperactivity disorder (ADHD) provided inconsistent concussion histories somewhat more frequently, compared with those without ADHD (7.8% and 3.5%, respectively; $p < 0.001$). Of the athletes with inconsistent concussion histories, greater degree of inconsistency was associated with a greater number of concussions initially reported at baseline ($rs = 0.54$; $p < 0.001$). Only a small proportion of student athletes provided inconsistent concussion histories. Male gender, ADHD, and greater number of baseline concussions were significantly associated with inconsistency in reporting. Overall, these findings suggest that student athletes are quite consistent when reporting their concussion history when surveyed twice during high school

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J Paediatr Child Health. 2017 Jan;53:55-61.

TRENDS IN PAEDIATRIC PRACTICE IN AUSTRALIA: 2008 AND 2013 NATIONAL AUDITS FROM THE AUSTRALIAN PAEDIATRIC RESEARCH NETWORK.

Hiscock H, Danchin MH, Efron D, et al.

AIM: In adult medicine, rates of investigation and prescribing appear to be increasing. Such information is lacking for paediatrics. We audited Australian paediatricians' practices in 2013 to determine changes since 2008 in: (i) conditions seen; (ii) consultation duration; (iii) imaging and pathology ordered; and (iv) prescribing. **METHODS**: This is a patient-level prospective audit of paediatricians' secondary care practice. Between November and December 2013, members of the Australian Paediatric Research Network were invited to complete standardised forms for 100 consecutive patients or all patients seen over 2 weeks, whichever was completed first. MAIN MEASURES: diagnoses, consultation duration, pathology and/or imaging investigations ordered, rate of medication prescription.

ANALYSES: hierarchical linear modelling clustered at the paediatrician level.
RESULTS: One hundred and eighty paediatricians (48% of those eligible) contributed 7102 consultations. The proportion of developmental/behavioural conditions rose from 48% (SD 31%) to 60% (SD 30%) in new and 54% (SD 28%) to 66% (SD 28%) in review consultations in 2013 compared with 2008. More paediatricians reported diagnoses of autism spectrum disorder (39-56%, P = 0.002), attention-deficit/hyperactivity disorder (47-55%, P = 0.05) and intellectual disability (18-36%, P = 0.001) in first consultations. Mean consultation duration and pathology/imaging ordering rates were stable. Prescribing rates increased from 39 to 45% of consultations for the top 10 new diagnoses and from 57 to 68% of consultations for the top 10 review diagnoses.
CONCLUSIONS: Paediatricians are seeing more children with developmental-behavioural conditions, prescribing more and demonstrating wide variation in their practice. The latter suggests both over- and under-treatment

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J Pain. 2017 Jan;18:29-41.
HEADACHE IMPAIRS ATTENTIONAL PERFORMANCE: A CONCEPTUAL REPLICATION AND EXTENSION.
Attridge N, Eccleston C, Noonan D, et al.
Pain is thought to capture our attention. A consequence is that our performance on other tasks may suffer. Research has supported this, showing that pain disrupts our ability to perform various attention tasks. However, the specific nature of the effect of pain on attention is inconsistent, possibly due to different studies investigating different types of pain. Few studies seek to replicate basic findings. In this study, we conceptually replicated and extended the headache study by Moore, Keogh, and Eccleston in 2013, by including 2 additional attention tasks, a broader sample, and measures of affect and pain cognition. Participants performed 5 complex attention tasks and a choice reaction time task with and without a naturally-occurring headache. Headache slowed reaction times to 4 of the 5 complex tasks, and this could be attributed to a slower basic processing speed measured using the choice reaction time task. Our findings differ from those of Moore et al in their headache study, suggesting that the effect of pain on attention is dynamic, even within a given type of pain. Whereas there is growing evidence that pain does disrupt attention, we cannot yet predict the specific nature of disruption in any given case.
PERSPECTIVE: We extended a study investigating the effect of headache on attention. Although both studies showed attentional disruption, the specific effects differed. Research must establish when and why the effect of pain on attention varies before we will be able to develop interventions to reduce attentional disruption from pain

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J Psychiatr Res. 2017 Jan;84:292-300.
MODAFINIL FOR THE TREATMENT OF ATTENTION-DEFICIT/HYPERACTIVITY DISORDER: A META-ANALYSIS.
Wang SM, Han C, Lee SJ, et al.
Attention-deficit/hyperactivity disorder (ADHD) is one of the most common and a debilitating neuro-behavior disorder in the pediatric population. Although numerous effective psychostimulants are available, more than 30% of patients still do not show adequate treatment response rendering diverse pharmacological options. We aimed at assessing the efficacy and safety of modafinil in the treatment of children and adolescents with ADHD by conducting a meta-analysis. An extensive search of databases and clinical trial registries resulted in five published short-term randomized, double-blind, placebo-controlled trials. Primary efficacy measures were mean change in ADHD Rating Scale-IV Home (ADHD-RS-IV Home) and School Version (ADHD-RS-IV School) from baseline to study end point. The results showed that modafinil more significantly improved ADHD-RS-IV Home (SMD, -0.77 [95%CI, -1.11 to -0.44]) and School (SMD, -0.71 [95%CI, -0.96 to -0.47]) than placebo. Dropout rate due to adverse event did not significantly differ between two groups. In terms of commonly observed side effects, modafinil showed significantly higher incidence of decreased appetite (RR = 5.02, 95% CIs, 2.55 to 9.89, P < 0.00001) and insomnia (RR = 6.16, 95% CIs, 3.40 to 11.17, P < 0.00001). Modafinil did not cause a clinically significant increase of heart rate, systolic blood pressure, and diastolic

blood pressure. Although we found that modafinil may be another treatment option in children and adolescents with ADHD, the results should be interpreted and translated into clinical practice with caution, as the meta-analysis was based on a limited number of clinical trials

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J Sch Health. 2017 Jan;87:47-54.

ETHNIC DISPARITIES IN SCHOOL-BASED BEHAVIORAL HEALTH SERVICE USE FOR CHILDREN WITH PSYCHIATRIC DISORDERS.

Locke J, Kang-Yi CD, Pellecchia M, et al.

BACKGROUND: We examined racial/ethnic disparities in school-based behavioral health service use for children with psychiatric disorders.

METHODS: Medicaid claims data were used to compare the behavioral healthcare service use of 23,601 children aged 5-17 years by psychiatric disorder (autism, attention deficit hyperactivity disorder [ADHD], conduct/oppositional defiant disorder, and "other") and by race/ethnicity (African-American, Hispanic, white, and other). Logistic and generalized linear regression analyses were used.

RESULTS: Differences in service use by racial/ethnic group were identified within and across diagnostic groups, both for in-school service use and out-of-school service use. For all disorders, Hispanic children had significantly lower use of in-school services than white children. Among children with ADHD, African-American children were less likely to receive in-school services than white children; however, there were no differences in adjusted annual mean Medicaid expenditures for in-school services by race/ethnicity or psychiatric disorders. Statistically significant differences by race/ethnicity were found for out-of-school service use for children with ADHD and other psychiatric disorders. There were significant differences by race/ethnicity in out-of-school service use for each diagnostic group.

CONCLUSIONS: Differences in the use of school-based behavioral health services by racial and ethnic groups suggest the need for culturally appropriate outreach and tailoring of services to improve service utilization

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J Child Adolesc Psychopharmacol. 2017;27:923.

ATOMOXETINE-RELATED TRICHOTILLOMANIA IN A BOY WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.

Akaltun I, Kara T.

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J Child Psychol Psychiatry. 2018 Jan;59:57-67.

WORKING MEMORY AND ORGANIZATIONAL SKILLS PROBLEMS IN ADHD.

Kofler MJ, Sarver DE, Harmon SL, et al.

Background: This study tested model-driven predictions regarding working memory's role in the organizational problems associated with ADHD.

Method: Children aged 8–13 (M = 10.33, SD = 1.42) with and without ADHD (N = 103; 39 girls; 73% Caucasian/Non-Hispanic) were assessed on multiple, counterbalanced working memory tasks. Parents and teachers completed norm-referenced measures of organizational problems (Children's Organizational Skills Scale; COSS).

Results: Results confirmed large magnitude working memory deficits (d = 1.24) and organizational problems in ADHD (d = 0.85). Bias-corrected, bootstrapped conditional effects models linked impaired working memory with greater parent- and teacher-reported inattention, hyperactivity/impulsivity, and organizational problems. Working memory predicted organization problems across all parent and teacher COSS subscales (R^2 = .19–.23). Approximately 38%–57% of working memory's effect on organization problems was conveyed by working memory's association with inattentive behavior. Unique effects of working memory remained significant for both parent- and teacher-reported task planning, as well as for teacher-reported memory/materials management and overall organization problems. Attention problems uniquely predicted

worse organizational skills. Hyperactivity was unrelated to parent-reported organizational skills, but predicted better teacher-reported task planning.
Conclusions: Children with ADHD exhibit multisetting, broad-based organizational impairment. These impaired organizational skills are attributable in part to performance deficits secondary to working memory dysfunction, both directly and indirectly via working memory's role in regulating attention. Impaired working memory in ADHD renders it extraordinarily difficult for these children to consistently anticipate, plan, enact, and maintain goal-directed actions

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J Consult Clin Psychol. 2018 Jan;86:39-55.

OVERCOMING THE RESEARCH-TO-PRACTICE GAP: A RANDOMIZED TRIAL WITH TWO BRIEF HOMEWORK AND ORGANIZATION INTERVENTIONS FOR STUDENTS WITH ADHD AS IMPLEMENTED BY SCHOOL MENTAL HEALTH PROVIDERS.

Langberg JM, Dvorsky MR, Molitor SJ, et al.

Objective: To evaluate the effectiveness of 2 brief school-based interventions targeting the homework problems of adolescents with attention-deficit/hyperactivity disorder (ADHD)—the Homework, Organization, and Planning Skills (HOPS) intervention and the Completing Homework by Improving Efficiency and Focus (CHIEF) intervention, as implemented by school mental health providers during the school day. A secondary goal was to use moderator analyses to identify student characteristics that may differentially predict intervention response.
Method: Two-hundred and eighty middle school students with ADHD were randomized to the HOPS or CHIEF interventions or to waitlist, and parent and teacher ratings were collected pre, post, and at a 6-month follow-up.
Results: Both interventions were implemented with fidelity by school mental health providers. Participants were pulled from elective periods and sessions averaged less than 20 min. Participants in HOPS and CHIEF demonstrated significantly greater improvements in comparison with waitlist on parent ratings of homework problems and organizational skills and effect sizes were large. HOPS participants also demonstrated moderate effect size improvements on materials management and organized action behaviors according to teachers. HOPS participants made significantly greater improvements in parent- and teacher-rated use of organized actions in comparison with CHIEF, but not on measures of homework problems. Moderation analyses revealed that participants with more severe psychopathology and behavioral dysregulation did significantly better with the HOPS intervention as compared to the CHIEF intervention.
Conclusions: Brief school-based interventions implemented by school providers can be effective. This type of service delivery model may facilitate overcoming the oft cited research-to-practice gap.
What is the public health significance of this article?—This study demonstrates that research developed interventions for youth with ADHD can be implemented in real world settings with integrity by typically trained school mental health providers. These interventions can be used to improve the homework and organization difficulties commonly experienced by youth with ADHD

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J Contemp Psychother. 2012;42:215-25.

TRANSPORTING A MANUALIZED TREATMENT FOR CHILDREN'S DISRUPTIVE BEHAVIOR TO A COMMUNITY CLINIC.

Shapiro JP, Youngstrom JK, Youngstrom EA, et al.

We compared a research-based, manualized intervention called Helping the Noncompliant Child (HNC; McMahon and Forehand 2003) to treatment as usual (TAU) for 194 children, 3ΓÇô9 years old, with disruptive behavior disorders in a community clinic. The two interventions did not produce different outcomes or levels of parent satisfaction. However, almost three times as many parents in the HNC condition stated they ended therapy because their goals had been met, and almost three times as many parents in TAU stated they terminated because of practical obstacles. Number of sessions was related to outcome in the HNC condition but not in TAU

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Journal of Learning Disabilities. 2018 Jan;51:55-72.

COMBINED MODALITY INTERVENTION FOR ADHD WITH COMORBID READING DISORDERS: A PROOF OF CONCEPT STUDY.

Tannock R, Frijters JC, Martinussen R, et al.

To evaluate the relative efficacy of two reading programs with and without adjunctive stimulant medication for children with attention-deficit/hyperactivity disorder and comorbid reading disorder (ADHD + RD). Sixty-five children (7–11 years in age) were assigned randomly to one of three intensive remedial academic programs (phonologically or strategy-based reading instruction, or general academic strategy and social skills training) in combination with either immediate-release methylphenidate or placebo. Multiple-blind procedures were used for medication/placebo, given twice daily. Children received 35 hours of instruction in 10 weeks, taught by a trained teacher in a separate school classroom, in small matched groups of 2 to 3. Children's behavior and reading abilities were assessed before and after intervention. Stimulant medication produced expected beneficial effects on hyperactive/impulsive behavioral symptoms (reported by classroom teachers) but none on reading. Children receiving a reading program showed greater gains than controls on multiple standardized measures of reading and related skills (regardless of medication status). Small sample sizes precluded interpretation of possible potentiating effects of stimulant medication on reading skills taught in particular reading programs. Intensive reading instruction, regardless of treatment with stimulant medication, may be efficacious in improving reading problems in children with ADHD+RD and warrants further investigation in a large-scale study

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Journal of Medicinal Food. 2017;20:1233-39.

THE EFFECT OF EXPERIMENTAL SUPPLEMENTATION WITH THE KLAMATH ALGAE EXTRACT KLAMIN ON ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.

Cremonte M, Sisti D, Maraucci I, et al.

Attention-deficit/hyperactivity disorder (ADHD) is a chronic neurobiological condition with onset in childhood. The disorder is characterized by inattention, impulsivity, and/or motor hyperactivity, which often affect the development and social integration of affected subjects. Phenylethylamine (PEA), naturally contained in the Klamath Lake microalgae and concentrated in the Klamin-« extract, is an endogenous molecule with a general neuromodulatory activity. It functions as an activator for the neurotransmission of dopamine and other catecholamines, and very low concentrations of PEA may be associated with specific psychological disorders such as ADHD. The aim of our study was to evaluate the efficacy of the Klamin extract in treating a group of subjects diagnosed with ADHD. Thirty subjects, aged 6-15, who had been diagnosed with ADHD according to the DSM-IV TR criteria, were enrolled. The supplement was administered to all the subjects, who reported to an ADHD clinic for routine follow-up visits. Observations were made and data collected over a 6-month period. After 6 months of therapy the subjects appeared to show significant improvements based on assessments of their overall functioning, behavioral aspects related to inattention and hyperactivity-impulsivity, attention functions in both the selective and sustained component and executive functions. The study appears to confirm the initial hypothesis that the Klamin extract may positively affect the expression of

ADHD symptoms. Additional larger studies on the effects of Klamin on ADHD are needed to further investigate the potential of this extract in ADHD treatment

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J Pediatr. 2012;161:A1.
ADHD IN PRETERMS.
Jobe AH.

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J Psychol Afr. 2017 Dec;27:541-44.
COMORBIDITY OF ATTENTION DEFICIT HYPERACTIVE DISORDER (ADHD) AND MAJOR DEPRESSION IN PRIMARY SCHOOL CHILDREN.
Mokobane M, Pillay B, Meyer A.
The study investigated comorbid Attention-Deficit/Hyperactivity Disorder (ADHD) and depression in a sample of rural primary school children in Limpopo Province, South Africa. A total of 320 learners participated in this study of whom 160 learners had teacher and parent identified ADHD symptoms (females = 50%; age range 6–14 years). All the learners took the Beck Depression Youth Inventory, second edition. Data were analysed applying ANOVA to investigate the possible differences between and within age, gender, and ADHD subtype group differences in depression symptomatology. Results indicated no statistically significant differences in the scores on the depression scale between the children with ADHD as identified by parents and teachers and the comparison group peers

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J Psychopathol Behav Assess. 2018;1-13.
PHYSIOLOGICAL EMOTION REGULATION IN CHILDREN WITH ADHD WITH AND WITHOUT COMORBID INTERNALIZING DISORDERS: A PRELIMINARY STUDY.
Leaberry KD, Rosen PJ, Fogleman ND, et al.
Children with Attention-Deficit/Hyperactivity Disorder (ADHD) experience deficits in emotion regulation that can be measured physiologically under environmental stress conditions by examining respiratory sinus arrhythmia (RSA), a marker of parasympathetic nervous system (PNS) withdrawal. The current pilot study examined the impact of comorbid internalizing disorders and comorbid Oppositional Defiant Disorder (ODD) on emotion regulation in children with ADHD by measuring RSA as an indicator of dysregulated emotional reactivity. Twenty-four 7ΓÇô10 year old children with ADHD participated in the current study. Children completed a 5-min resting attending baseline while electrocardiogram data (ECG) were recorded to examine baseline RSA. Children then completed a stress inducing, blocked goal, Card Sorting Task to measure RSA reactivity to stress. Results revealed a significant effect of internalizing disorder status on RSA difference score, F (1, 18) = 5.83, p = .03, +À2 = .25. Children in the comorbid internalizing disorder group had a significantly greater decrease in RSA from the baseline time period to the card sorting task. There was no significant effect of ODD diagnostic status on RSA difference score, p > .05. The results of this preliminary study suggest that among children with ADHD, the presence of a comorbid internalizing disorder predicts greater withdrawal of the PNS. These findings represent an important step in understanding autonomic functioning of children with ADHD and comorbid disorders

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J Psychother Integr. 2017;27:526-39.

A PILOT FEASIBILITY STUDY OF INTERPERSONAL PSYCHOTHERAPY IN ADOLESCENTS DIAGNOSED WITH SPECIFIC LEARNING DISORDERS, ATTENTION DEFICIT HYPERACTIVE DISORDER, OR BOTH WITH DEPRESSION AND/OR ANXIETY SYMPTOMS (IPT-ALD).

Brunstein-Klomek A, Kopelman-Rubin D, Apter A, et al.

Specific learning disorders (SLD) significantly interfere with academic functioning and interpersonal relationships and often co-occur with attention deficit/hyperactivity disorder (ADHD), depression, and anxiety symptoms. Most of the interventions for SLD adolescents have focused on enhancing cognitive and learning skills. Interpersonal psychotherapy for depressed adolescents (IPT-A) is a time-limited, evidenced-based psychotherapy for depressed adolescents. It combines interpersonal, emotional, and behavioral work. This is the first study to examine the feasibility and acceptability of IPT-A adapted for adolescents diagnosed with SLD, ADHD, or both with depression and anxiety symptoms (IPT-ALD). The participants consisted of 18 adolescents who started the treatment, ages 10-17 years (mean 12.57) while 15 completed the intervention. Seven out of the 15 completers were followed up after 3 months. The intervention included 15 weekly sessions and 3 follow-up sessions. The skills-based intervention focuses on an identified problem area and aims to improve the adolescent's coping with their SLD/ADHD challenges; reduce anxiety and depression symptoms; and improve interpersonal and social functioning. Results indicated that IPT-ALD is a feasible treatment to deliver with high satisfaction. Attachment to mother and school avoidance significantly improved from beginning to end of acute treatment. At 3-month follow-up, youths' self-reports indicated fewer general difficulties and more significant improvement in generalized anxiety, separation anxiety, social phobia, and school avoidance. Improvement at the 3-month follow-up indicated that some of the changes for these youths may have a delayed impact. Future studies should examine the effectiveness of the intervention in a randomized control trial

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J Am Acad Child Adolesc Psychiatry. 2017;56:S176-S177.

TRIAL OF POSITIVE PSYCHIATRY IN COMORBID ATTENTION-DEFICIT HYPERACTIVE/DISORDER (ADHD) WITH POSTTRAUMATIC STRESS DISORDER (PTSD).

Ahmadi N, Chaudhry S, Salam T, et al.

Objectives: ADHD is associated with higher levels of morbidity and dysfunction, especially in those with PTSD. Recent studies revealed that positive psychiatry (PP) can decrease symptoms of adversity and psychopathology and increase the well-being in youth. This study investigates the impact of PP on vascular function, inflammation, well-being, and ADHD and PTSD symptoms in adolescents with comorbid ADHD and PTSD.

Methods: Eleven adolescents (age = 11 -¦ 3 years; range = 10-15 years; 50% female), after obtaining informed consent, were randomized to the PP group (n = 5) or CBT group (n = 6). Eight participants (PP, n = 4; CBT, n = 4) completed a six-week trial. Vascular function measured as temperature rebound by reactive hyperemia, C-reactive protein (CRP), homocysteine, and neuropsychiatric measures [i.e., SNAP (Special Needs and Autism Project) questionnaire; PERMA (positive emotion, engagement, relationships, meaning and accomplishment); gratitude; posttraumatic growth inventory; Connor-Davidson Resilience Scale; and Clinician-Administered PTSD Scale (CAPS), children version] were measured at baseline and at week six.

Results: At follow-up, a significant improvement in CAPS-CA, SNAP, and vascular function of both PP and CBT groups was noted compared with baseline that was more robust in the PP group ($P < 0.01$). At week six, a significant decrease in homocysteine and CRP, as well as an increase in PERMA, gratitude, resilience, and posttraumatic growth inventory scores in PP group, but not in CBT group, was noted ($P < 0.01$). A significant relationship between a decrease in CAPS and SNAP scores and an increase in vascular function, as well as a decrease in homocysteine, were noted ($P < 0.01$). Furthermore, A direct relationship between increase in PERMA, gratitude, resilience, and posttraumatic growth inventory scores, with increase in vascular function and decrease in homocysteine, was noted ($P < 0.01$). The most robust improvement was noted in positive connectedness, including new possibilities, appreciation of life, personal strength, and relating to others ($P < 0.01$).

Conclusions: PP is associated with improving PTSD and ADHD symptoms, as well as increase in well-being and vascular function, and reducing inflammation in adolescents with comorbid ADHD and PTSD. This

highlights the importance the dual role of PP in addressing vulnerable symptoms, as well as enhancing well-being in youth with ADHD and PTSD

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J Am Acad Child Adolesc Psychiatry. 2017;56:S322.

THE DEVELOPMENT OF DEPRESSION IN CHILDREN WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER: EXPLORING THE IMPACT OF PUBERTAL DEVELOPMENT AND TREATMENT EFFECTS IN GIRLS VERSUS BOYS.

Babinski DE, Waschbusch D, Waxmonsky JG.

Objectives: Girls with ADHD are at risk for depression. However, not all girls with ADHD develop mood problems; thus, identification of factors that exacerbate or mitigate the risk for depression is needed. Early pubertal development may exacerbate the risk for depression among girls with ADHD, whereas treatment of ADHD may mitigate the risk for depression. This study examines the effects of early puberty and treatment of ADHD on risk for depression in girls and boys with ADHD.

Methods: Data from the Multimodal Treatment of ADHD (MTA) Study were used. The MTA is a trial (n = 579) of three treatments (stimulant medication, behavioral, and their combination), as well as a community control, delivered over a 14-month period to children with ADHD. A group of 289 children without ADHD was also recruited. To examine early puberty effects on depression, data collected 36 months after the initial treatment initiation (i.e., preadolescence) were used. Self-reports of depression, parent and teacher reports of ADHD severity, and self-ratings of pubertal status were collected from children and a study nurse when available. ADHD x gender x puberty effects on depression were examined with regression. The effects of treatment and gender on the development of depression were examined into adulthood using mixed models.

Results: A significant ADHD x gender x puberty interaction emerged for depressive symptoms ($F = 5.87$, $P < 0.01$). Simple slopes tests showed that among girls with ADHD, early versus later puberty was associated with greater depression ($b = 1.65$, $P < 0.05$), whereas early versus later puberty was associated with lower depression among boys with ADHD ($b = -2.32$, $P < 0.05$) and remained significant when controlling for symptoms of oppositional defiant disorders. Regarding treatment x gender effects, findings point to potential benefits of behavioral treatment versus stimulant medication treatment, particularly for girls versus boys with ADHD.

Conclusions: Our findings fit with previous work showing that childhood adversity accentuates the negative impact of early puberty in girls. Gender x treatment effects offer the promise that intervention for ADHD may attenuate risk for depression in girls

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J Am Acad Child Adolesc Psychiatry. 2017;56:S59.

CAREGIVER KNOWLEDGE AND ATTITUDE TOWARD MENTAL HEALTH PROBLEMS IN CHILDREN IN CHICAGO, ILLINOIS, AND WUHAN, CHINA.

Afzal KI.

Objectives: The purpose of this study is to 1) review the University of Chicago Behavioral Health Questionnaire (UCBHQ); and 2) understand parental attitude toward seeking mental health (MH) services for children from Chicago's immigrant population and the general population in Wuhan, China.

Methods: A total of 93 participants in Chicago, Illinois were included.

Results: Compared with Arab-Americans, Asian-Americans believed that ADHD was not a mental illness ($P < 0.004$) and that behavioral or mental health problems were present in the Western cultures and not Eastern cultures ($P < 0.002$). Males generally believed that anxiety and ADHD were not medical and/or mental illnesses ($P < 0.03$ and $P < 0.017$), respectively. Compared with their counterparts, female respondents believed that behavioral problems in children were a part of MH ($P < 0.002$); however, they were less likely to believe that behavioral issues were a part of MH in teenagers ($P < 0.018$). Men were more likely to believe that medications/therapy change brain chemistry ($P < 0.001$). Respondents who had been living in the United States for more than 15 years were more likely to believe that behavioral/MH conditions were caused by chemical imbalance in the brain ($P < 0.035$) and that medications/therapy change the chemistry of the brain ($P < 0.02$), compared with respondents who had been living in the United States for a fewer number of years.

Southeast Asians were more likely to believe that behavioral or MH conditions are only present in the Western cultures and not Eastern cultures (P < 0.005), compared with their contemporaries who spent their youth in the United States.
Conclusions: Addressing cultural influences on stigma empowers mental health providers to effectively deliver culturally sensitive services and to improve adherence

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J Am Acad Child Adolesc Psychiatry. 2017;56:S94.
PREADOLESCENT MOODINESS AND ATTENTION-DEFICIT/HYPERACTIVITY DISORDER: EFFECTIVE STRATEGIES FOR ASSESSMENT AND TREATMENT.
Daviss WB, Walkup JT.
Objectives: Participants will learn practical strategies for accurately assessing various psychiatric causes of moodiness/irritability in childhood ADHD, including comorbid autism spectrum disorder (Dr. McLaren), anxiety and OCD (Dr. Spaniardi), PTSD (Dr. Daviss), and disruptive behavioral disorders, including ODD, conduct, and disruptive mood dysregulation disorders (Dr. Blader). Participants will also learn potentially effective strategies for pharmacological and psychosocial treatments of such mood and behavioral problems in children with ADHD
Methods: Each of the above speakers will review practical ways to assess such children, including interview tips and use of rating scales. They will also summarize the literature regarding pharmacological and psychosocial treatments for these comorbid mood problems, including recommendations from consensus panels of experts when available. Handouts of the PowerPoint slides and other helpful materials will also be made available to participants on-line. Dr. John Walkup, an internationally recognized child and adolescent psychiatrist researcher, will serve as a discussant, highlighting key points of the other presenters, and their potential relevance to clinicians and clinical researchers alike.
Results: Through these presentations and subsequent discussions, participants will improve their working knowledge of how to assess and treat these various causes of moodiness or irritability in their child patients with ADHD.
Conclusions: Attendees of this clinical presentation will feel more capable in diagnosing and treating children with ADHD and these other mood and behavioral problems and also will be aware of the knowledge gaps in this field that future research will need to fill

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J Am Acad Child Adolesc Psychiatry. 2017;56:S95.
TRAUMA-RELATED MOODINESS IN CHILDREN WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.
Daviss WB.
Objectives: Patients with ADHD of all ages often experience traumatic events and may display moodiness as a result, even without having fullblown PTSD. Participants will learn practical strategies to screen for traumatic exposure and trauma-related symptoms in children with ADHD and potential strategies for using psychosocial and pharmacological treatments in such patients.
Methods: Based on a review of the PTSD and ADHD literature, the speaker will discuss risks related to traumatic exposure and PTSD in children with ADHD and the biological basis of pediatric stress responses. He will then review practical strategies for identifying trauma exposure and its signs and symptoms in patients with ADHD. Finally, he will review the literature supporting pharmacological and especially psychosocial treatments for trauma-related psychopathology and how such treatments can be applied to traumatized children with ADHD.
Results: There are many shared risk factors for ADHD and trauma exposure. Symptoms related to trauma exposure, including re-experiencing, avoidance, depressive, and hyperarousal symptoms, are easily confused with the symptoms of ADHD and its comorbidities. Traumarelated symptoms may alter such children's neurobiology and impair their ability to function or respond to standard treatments for ADHD. There is strong evidence in children supporting pharmacological treatments for ADHD and trauma-focused CBT

(TF-CBT) for PTSD. Evidence for PTSD pharmacotherapy (including SSRIs, a agonists, atypical antipsychotic drugs, and Prazosin) is more limited and mostly from studies in adults.
Conclusions: Based on the available evidence, clinicians should generally first offer psychosocial treatments for the PTSD, such as TF-CBT and/or pharmacological treatment of the ADHD, and then consider adding other pharmacotherapy for more refractory or severe cases of PTSD symptoms in such patients

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J Am Acad Child Adolesc Psychiatry. 2017;56:S279.

STUDY OF VARIABLES AFFECTING ATTENTION-DEFICIT/HYPERACTIVITY DISORDER (ADHD) AND ASTHMA COMORBIDITY.

Desai T, Periasamy M, Nguyen D-T, et al.

Objectives: ADHD and asthma are chronic pediatric illnesses with prevalence rates of 11 and 8.4 percent, respectively. Their comorbidity needs further consideration in terms of how demographic and clinical measures, such as age, gender, race, birth weight, socioeconomic status, association with sleep disorder, and ADHD subtype, impact it. Understanding the impact of such variables on manifestation of ADHD and asthma symptoms may enhance our understanding of its outcome.
Methods: This retrospective chart review includes data from 622 patients (ages 2-18 years) with ADHD from the Child Psychiatry Clinic at the University of Virginia. Data points analyzed include age, sex, race, onset of diagnosis, type of ADHD, ADHD and asthma medications, sleep symptoms, sleep disorder diagnosis, and presence of asthma. Statistical analyses were performed using SAS version 9.4 and include means, Chi-square (c2) tests, and 95 percent confidence intervals.
Results: Approximately 19.13 percent (n = 119) of the population had a comorbid diagnosis of asthma, which is higher than the number reported by the CDC (8.4%). Children with asthma were more likely to have sleep symptoms (c2 = 6.54, P = 0.01). When controlling for gender, females were more likely to present with asthma and sleep symptoms (c2 = 3.84, P = 0.05) than males (c2 = 3.02, P = 0.08). Children with a mixed ADHD subtype were more likely to present with asthma and sleep symptoms (c2 = 8.01, P = 0.005) than other subtypes. African Americans were less likely to have sleep symptoms (c2 = 4.42, P = 0.04) and even less likely if they did not have asthma (c2 = 5.11, P = 0.02). Amphetamine use was significantly linked to asthma (c2 = 5.54, P = 0.02, 95% CI = 0.05-0.45). Asthmatics on amphetamines were less likely to have sleep symptoms (c2 = 7.73, P = 0.005) or a sleep disorder diagnosis (c2 = 3.59, P = 0.06). Nonasthmatic patients on ADHD medications were more likely to not have a sleep disorder diagnosis (c2 = 6.46, P = 0.01).
Conclusions: The higher prevalence of asthma in children with ADHD shows the need to further examine this relationship. Gender and ADHD subtype impact children who present with both asthma and sleep symptoms. The response differs in African Americans compared with other races. This study also highlights the significance of appropriate ADHD and asthma treatments with existing sleep symptoms in the presence or absence of asthma

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J Am Acad Child Adolesc Psychiatry. 2017;56:S76.

MOODINESS IN ADOLESCENTS AND ADULTS WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER: STRATEGIES FOR ASSESSMENT AND TREATMENT.

Daviss WB, Birmaher B.

Objectives: Participants will learn practical strategies for accurately assessing various psychiatric causes of moodiness/irritability in childhood ADHD, including comorbid autism spectrum disorder (Dr. McLaren), anxiety and obsessive-compulsive disorder (Dr. Spaniardi), PTSD (Dr. Daviss), and disruptive behavioral disorders, including oppositional defiant, conduct, and disruptive mood dysregulation disorders (Dr. Blader). Participants will also learn potentially effective strategies for pharmacological and psychosocial treatments of such mood and behavioral problems in children with ADHD.
Methods: Each of the above speakers will review practical ways to assess such children, including interview tips and use of rating scales. They will also summarize the literature regarding pharmacological and psychosocial treatments for these comorbid mood problems, including recommendations from consensus

panels of experts when available. Handouts of the PowerPoint slides and other helpful materials will also be made available to participants online. Dr. John Walkup, an internationally recognized child and adolescent psychiatrist researcher, will serve as a Discussant, highlighting key points of the other presenters and their potential relevance to clinicians and clinical researchers alike.
Results: Through these presentations and the subsequent discussions and period of questions and answers, participants will improve their working knowledge of how to assess and treat these various types of mood problems in children with ADHD.
Conclusions: Attendees of this clinical presentation will feel more capable in diagnosing and treating young patients with ADHD with these comorbid mood and behavioral problems and be aware of the knowledge gaps in field that will necessitate future research

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J Am Acad Child Adolesc Psychiatry. 2017;56:S218.
THE RELATION OF PARENT-CHILD INTERACTION THERAPY (PCIT) IN WELL-BEING OF YOUNG CHILDREN WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER (ADHD) AND OPPOSITIONAL DEFIANT DISORDER.
Ahmadi N, Chaudhry S, Olango G, et al.
Objectives: Previous studies have demonstrated effectiveness of Parent-Child Interaction Therapy (PCIT) in improving children's disruptive behavioral problems. This study investigates the effect of PCIT on the well-being of young children with ADHD and ODD.
Methods: Eleven consecutive children (ages 5-8 years, 7 males) who scored 120 on the Eyberg Child Behavior Inventory (ECBI) received PCIT. The child and families were assessed at baseline and at four months after beginning treatment. Parenting skills were measured using the Dyadic Parent-Child Interaction Coding System (DPICS), and child behavior problems were measured using the ECBI and the Child Behavior Checklist (CBCL). Well-being was measured using multidimensional PERMA model (positive emotions, engagement, positive relationships, meaning, and accomplishment). Wellbeing was defined as low (PERMA score 3), average (PERMA score 4-5), and high (PERMA score 6).
Results: At follow up, after PCIT intervention, a significant improvement in children's behavior (ECBI baseline: 147 22 vs. follow-up: 80 15, P = 0.001) and parents' do and don't skills, measured by observer rating on DPICS (d = 2.9, d = 1.6, respectively, P = 0.01), were noted. The total PERMA score, as well as scores in each dimension, were significantly improved at follow-up in both children and parents compared with baseline (P = 0.01). The most robust improvement was noted in positive relationships, engagements, and accomplishments (P < 0.05).
Conclusions: The current findings reveal that PCIT is associated with an increase in well-being of both children and parents, in addition to significant reduction of children's disruptive behavior. This highlights the importance of simultaneous intervention to address vulnerable symptoms, as well as enhancing well-being in youth with ADHD and ODD

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J Am Acad Child Adolesc Psychiatry. 2017;56:S207.
PARENT-REPORTED BENEFITS AND SIDE EFFECTS FROM ATTENTION-DEFICIT/HYPERACTIVITY DISORDER (ADHD) MEDICATION IN A NATIONALLY DRAWN SAMPLE OF SCHOOL-AGED CHILDREN DIAGNOSED WITH ADHD.
Holbrook J, Danielson M, Bitsko RH, et al.
Objectives: The purpose of this study is to characterize the magnitude of perceived benefits and side effects associated with ADHD medication use in a nationally drawn sample of school-aged children with ADHD.
Methods: We analyzed data from the National Survey of the Diagnosis and Treatment of ADHD and Tourette Syndrome (NS-DATA; N = 2,980). Among children with parent-reported ADHD, parents reported on side effects for those who had ever taken ADHD medication; parents also reported on benefits of medication for children currently taking ADHD medication. SUDAAN version 11.0.1 was used for all analyses to account for the complex sampling design and sampling weights.
Results: Among children with a parent-reported ADHD diagnosis, 88 percent (n = 2,647) had ever used ADHD medication; 74 percent (n = 1,752) were currently taking medication. Most children who had ever

taken a medication (92%) had experienced one or more of the 11 types of side effects specified in the survey; 68 percent had experienced at least three side effects. The most commonly reported side effects were change in personality or mood (56%) and sleep problems (54%). Side effects were more common in boys, children diagnosed before age six years, children with severe ADHD, and those with a co-occurring condition. Although 48 percent of medication users had experienced side effects troublesome enough for the parent to discontinue the child's medication, 56 percent of children whose medication use was discontinued due to side effects were currently using medication. Among children currently taking ADHD medication, most parents reported at least some improvement with academics (91%), behavior (89%), and interactions with others (79%); 72 percent reported at least some improvement in all three domains. Parents not reporting a side effect were more likely to report a lot of improvement (compared to some, a little, or none) in academics (81% vs 68%; p = 0.02), behavior (73% vs 56%; p < 0.01), and interactions (62% vs 41%; p < 0.01).
Conclusions: This study quantifies the proportion of children experiencing benefits and side effects of ADHD medication in a nationally drawn sample. The vast majority of children taking ADHD medication experience significant benefit across areas of daily life, but most also experience multiple side effects. These data can be used by clinicians and shared with families to help balance the benefits of medication with the risks of known side effects

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J Am Acad Child Adolesc Psychiatry. 2017;56:S282.

CAREGIVER-REPORTED SIDE EFFECTS OF METHYLPHENIDATE AND COMORBID OPPOSITIONAL DEFIANT DISORDER DIAGNOSIS IN CHILDREN WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER (ADHD).

Hsu S, Piedra AN, Froehlich TE, et al.

Objectives: Prior studies on methylphenidate (MPH) and children with ADHD and comorbid oppositional defiant disorder (ADHD+ODD) have mainly focused on MPH efficacy in reducing ADHD symptoms. Although decreased MPH adherence has been shown in children with ADHD+ODD, and side effects are known to adversely affect adherence, little is known about the influence of comorbid ODD on MPH side effects. This study aims to investigate the relationship between caregiver-reported side effects in children with ADHD alone versus ADHD+ODD.
Methods: Stimulant-na+»ve children with ADHD (N = 170, aged 7-11 years) completed a four-week randomized double-blind, placebo-controlled trial of long-acting MPH with three fixed active dosages (low, medium, and high). Based on the Diagnostic Interview Schedule for Children, 45 children had comorbid ODD. Before starting MPH (baseline) and after each dosage and placebo week, caregivers rated common side effects using the Pittsburgh Side Effect Rating Scale (0 = never, 1 = occasionally, 2 = often, and 3 = very often). We used Chi-square tests to compare caregiver side effect ratings (0 = absent vs. 1, 2, or 3 = present) in children with ADHD only versus ADHD+ODD.
Results: At baseline, children with ADHD+ODD had higher anxiousness (P < 0.001), stomachache (P = 0.001), irritability (P < 0.001), depression (P < 0.01), social withdrawal (P < 0.001), and trouble sleeping (P = 0.001) than children without ODD. During week of placebo administration, children with ADHD+ ODD had higher parent ratings of irritability (P = 0.007) than the children without ODD. However, during the high dose of MPH week, there were no differences in caregiver-reported side effects in children with versus without comorbid ODD (all P > 0.1).
Conclusions: At premedication baseline, and to some extent on placebo, children with ADHD+ODD had higher caregiver-reported ratings of emotional and somatic complaints compared with those with ADHD only. However, this difference was not seen during the MPH high-dose week, suggesting that the reduced MPH adherence observed in children with comorbid ADHD and ODD is not driven by higher levels of side effects experienced in this group

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J Am Acad Child Adolesc Psychiatry. 2017;56:S62-S63.

PROBING THE BOUNDARIES OF THE ATTENTION-DEFICIT/HYPERACTIVITY DISORDER SPECTRUM AND REQUESTS FOR ITS TREATMENTS AS NEUROENHANCEMENT.

Graf W.

Objectives: The goal of this session is to review the variance in ADHD prevalence and demographics and the imperative of clinical guidelines in its diagnosis and treatment.

Methods: We reviewed existing data on ADHD diagnostic prevalence and the striking discrepancies between medical specialties, cultures, geographical areas, and age groups. In addition, we reviewed recent data on current trends in stimulant medication prescription and diversion. We assessed the ADHD diagnosis as a neurodevelopmental spectrum disorder and compared its consequences to other spectrum disorder diagnostic constructs. We examined recent data on smart drugs, their markets, efficacy, potential harm, and user intent and discuss the ethical and legal responsibilities to patients with ambiguous ADHD complaints who are prescribed stimulants to enhance cognitive or affective functioning.

Results: The nosological justification of behaviorally and dimensionally defined spectrum disorders is an inclusive classification scheme allowing overlapping heterogeneous conditions, regardless of severity or etiology. As a consequence, spectrum disorders lack strictly demarcated diagnostic boundaries. ADHD becomes a controversial diagnosis when its signs and symptoms are mild or ambiguous. Recent statistics indicate that almost half (46.7%) of US children diagnosed with ADHD have mild problems and that only about one in six children diagnosed with ADHD have severe impairment. Despite efforts to implement dimensionality, pragmatic coupling of any broad categorical diagnosis to its designated interventions is a continuing challenge.

Conclusions: Neither the acknowledgement of ADHD dimensionality, nor the application of the impairment criterion is addressing the problem of appropriate diagnosis and management of ADHD symptoms and behaviors in various age groups. Current trends of stimulant drug use compel ongoing discussions about these topics

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J Am Acad Child Adolesc Psychiatry. 2017;56:S95-S96.

OPPOSITIONAL/CONDUCT AND DISRUPTIVE MOOD DYSREGULATION DISORDERS AND ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.

Blader JC.

Objectives: Childhood ADHD with affective disturbances that lead to harmful behavior is highly prevalent, but uncertainties in its understanding and treatment persist. This presentation focuses on three common interacting pathogenic factors: generalized impulse control deficits; several affective processes that require careful assessment; and social and environmental factors that affect symptom expression and impairment. Dyscontrolled behavior driven by extreme emotional states is common among children with ADHD. However, key aspects have long eluded consensus, including the underlying psychopathology, diagnostic approaches, and optimal treatment. The controversies are largely reducible to differences in attributing these behaviors primarily to global self-control problems or to an identifiable mood disorder.

Methods: We start with a brief historical review of diagnostic approaches to impulsive youth with high emotional lability. Case vignettes will illustrate common clinical uncertainties. Drawing on recent studies, we will present the rationale for a suggested algorithm for assessment and treatment. Factors that may hamper optimal treatment in community clinical settings will be discussed.

Results: This presentation converges on three main points. First, weak self-regulatory processes emblematic of ADHD often lead to high negative emotional reactivity without invoking a separate mood disorder. Second, avid pursuit of first-line treatments that could alleviate these problems for most affected youth seem underutilized in practice, and there are some external barriers to doing so. Third, our current diagnostic schema has not kept pace with scientific developments in emotion and its regulation.

Conclusions: The interface between impulse control and emotional processes is complex, but current tools make the resulting impairments tractable in many clinical situations. Obstacles to using them in a timely fashion need to be addressed

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J Am Acad Child Adolesc Psychiatry. 2017;56:S165.

EFFICACY AND SAFETY OF SHP465 MIXED AMPHETAMINE SALTS IN CHILDREN AND ADOLESCENTS WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER (ADHD): A RANDOMIZED, PLACEBO-CONTROLLED STUDY.

Brams M, Childress A, Greenbaum MS, et al.

Objectives: The goal of this study is to evaluate the efficacy, tolerability, and safety of SHP465 mixed amphetamine salts (MAS) in children and adolescents with ADHD.

Methods: This randomized, double-blind, placebo (PBO)-controlled, doseoptimization study enrolled children and adolescents (ages 6-17 years) with DSM-IV-Text Revision-defined ADHD and baseline ADHD Rating Scale IV (ADHD-RS-IV) total scores 28. Participants from 36 US clinical research sites were randomized 1:1 to SHP465 MAS [week 1: 12.5 mg; week 2: titrated to 25 mg based on efficacy, safety, and tolerability; weeks 3-4: the final titrated dose (12.5 or 25 mg) was maintained] or PBO. The primary (ADHD-RS-IV total score change from baseline to week 4) and key secondary [Clinical Global Impressions-Improvement (CGI-I) score at week 4] efficacy endpoints were assessed using linear mixed-effects models for repeated measures. Safety and tolerability, including treatment-emergent adverse events (TEAEs) and vital sign changes, were examined descriptively.

Results: Of 264 randomized participants (PBO, n = 132; SHP465 MAS, n = 132), 29 were discontinued from the study (PBO, n = 13; SHP465 MAS, n = 16). The least squares (LS) mean (95% CI) ADHD-RS-IV total score change from baseline to week four was significantly greater with SHP465 MAS than PBO [-20.7 (-22.9,-18.5) vs.-10.8 (-13.0,-8.5); P < 0.001; effect size = 0.80]. The LS mean (95% CI) CGI-I score at week four was significantly lower (indicating greater improvement) with SHP465 MAS than PBO [2.2 (2.0, 2.4) vs. 3.0 (2.8, 3.2); P < 0.001; effect size = 0.65]. The frequency of TEAEs was 46.6 percent (61/131) with PBO and 67.4 percent (89/132) with SHP465 MAS. TEAEs reported at a frequency of 10 percent (SHP465 MAS; PBO) were decreased appetite (30.3%; 6.9%), headache (12.1%; 10.7%), and insomnia (11.4%; 1.5%). Mean ± SD changes from baseline at the final on-treatment assessment for SHP465 MAS and PBO, respectively, were 5.7 ± 11.78 and 0.7 ± 10.79 beats per minute for pulse, 3.8 ± 9.15 and 2.1 ± 8.72 mm Hg for systolic blood pressure, and 4.0 ± 8.23 and 0.5 ± 7.45 mm Hg for diastolic blood pressure.

Conclusions: SHP465 MAS was superior to PBO in reducing ADHD symptoms and improving global functioning in children and adolescents with ADHD. The safety and tolerability profile of SHP465 MAS was consistent with the known profiles of other stimulants

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J Am Acad Child Adolesc Psychiatry. 2017;56:S278.

PILOT STUDY OF THE EFFECT OF ATTENTION-DEFICIT/HYPERACTIVITY DISORDER (ADHD) ON CHILD ASTHMA: AUTONOMIC NERVOUS SYSTEM DYSREGULATION AS A MEDIATOR?

Chankalal RR, Quratulain H, Kaur S, et al.

Objectives: Childhood asthma and ADHD co-occur more frequently than their individual prevalence rates, with asthma disease severity being worse in these populations. The underlying cause of this is not known. There is evidence for autonomic nervous system (ANS) dysregulation in both stressinduced compromise of pulmonary function in asthma and in ADHD. We assessed ANS dysfunction, in particular vagal reactivity, as a possible mechanism by which ADHD could worsen child asthma because vagal/cholinergic mechanisms mediate airway constriction. We tested these hypotheses: 1) children with asthma plus ADHD have greater asthma disease severity, worse pulmonary function, and greater vagal reactivity compared to children with asthma alone; and 2) greater asthma disease severity and worse pulmonary function are associated with greater vagal reactivity.

Methods: A secondary analysis was conducted using a data set obtained from children aged 7-17 years (n = 106) who presented to an emergency department for asthma exacerbation. Two gender-matched groups were identified based on ADHD t-scores: asthma (A), < 60th percentile, and asthma plus ADHD (A+ADHD) >69th percentile. We compared the two groups for asthma disease severity, pulmonary function, and ANS function. Pulmonary function and ANS function were monitored throughout selected scenes of an emotionally stressful film. Sympathetic and vagal ANS reactivity were measured for these scenes.

Results: Correcting for the contribution of depression (which is known to worsen pulmonary function and disease severity in childhood asthma), there was worse pulmonary function and disease severity in the A+ADHD group (p < 0.06, p < 0.05, respectively). Vagal reactivity was significantly greater for the A+ADHD

group during the death scene ($p < 0.05$). Greater asthma disease severity was significant ($p = 0.03$) but weakly correlated ($r = 0.19$) to ADHD severity. There were no significant correlations for vagal reactivity and pulmonary function with ADHD severity.
Conclusions: Children with asthma plus ADHD are at risk for more severe and unstable asthma, which may be mediated by increased vagal reactivity. Identification of ADHD in children with asthma may be of benefit in monitoring their asthma control, especially under conditions of emotional distress

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J Am Acad Child Adolesc Psychiatry. 2017;56:S238-S239.
IRRITABILITY AND LIMITED PROSOCIAL EMOTIONS/CALLOUS-UNEMOTIONAL TRAITS IN ELEMENTARY SCHOOL-AGE CHILDREN WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER (ADHD) AND CONDUCT PROBLEMS.
Baweja R, Waxmonsky JG, Babinski DE, et al.
Objectives: Conduct problems (CP) are highly heterogeneous within and across children, and numerous efforts have been made to use affective traits to better specify the nature of conduct problems. Two primary approaches in this regard are presence of irritability (IRR) and the presence of limited prosocial emotions/callous-unemotional traits (LPE/CU). This study examined the association between IRR and LPE/CU among elementary school age children with serious conduct problems.
Methods: Participants were 123 children (102 boys, mean age = 9.73 years), who met criteria for ODD and ADHD (47.2%) or conduct disorder (CD) and ADHD (52.8%). Diagnoses were assigned using DSM-IV-Text Revision (TR) criteria as assessed by several sources of information, including ratings completed by parents and teachers and a structured diagnostic interview administered to parents. The Antisocial Process Screening Device was completed to assess CU traits. The Disruptive Behavior Disorder Rating Scale was completed to assess symptoms of CD, ODD, and ADHD. The Child Behavior Checklist (CBCL) and Teacher Report Form (TRF) were completed to examine anxious-depressed, withdrawn-depressed, social problems, attention problems, rule breaking, and aggressive behavior outcomes. The Nova Scotia Modified IOWA Conners was completed to measure aggression and peer relationships in children.
Results: Within this sample, youth met criteria for both IRR and LPE/CU (30.1% both), IRR but not LPE/CU (26.8% IRR-only), LPE/CU but not IRR (18.7% LPE/CU-only), and neither IRR nor LPE/CU (24.4% neither). Results showed that IRR and LPE/CU were not correlated ($r = 0.09$, $p = 0.306$) and categorical analyses showed that only half of the children with IRR had LPE/CU and half of the children with LPE/CU had IRR. Comparisons of LPE/CU-only, IRR-only groups, both LPE/CU and IRR, and neither condition showed groups differed in meaningful ways on measures of psychopathology, aggression, and social functioning.
Conclusions: These findings suggest that IRR and LPE/CU may represent distinct phenotypes within children with conduct problems. Results suggest that future research and treatment of children with conduct problems may benefit from simultaneously taking into account IRR and LPE

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J Am Acad Child Adolesc Psychiatry. 2017;56:S279.
DIFFERENTIAL PATTERNS OF SUICIDE IDEATION, DEPRESSIVE, AND ANXIETY SYMPTOMS IN SCHOOL-AGE YOUTHS WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER (ADHD).
Choi B-S, Kim J-H, Huh SY, et al.
Objectives: Suicide is associated with mood disorders, substance abuse and addiction, personality disorders, and psychiatric disorders. ADHD is one risk factor for suicide. ADHD and suicidal behavior are common conditions with significant social and emotional morbidity. The purpose of this study is to investigate differential patterns of suicide ideation and depressive and anxiety symptoms in school-age youths with ADHD.
Methods: The subjects were divided into a patient group and a control group. The patient group included 49 patients diagnosed with ADHD in the department of psychiatry of one university hospital. For the control group, 3,727 youths in elementary schools, middle schools, and high schools in the metropolitan city of Busan were asked to fill out questionnaires. Of the 1,717 respondents to the questionnaires, 245 were selected for patient-controlled studies. All of the subjects were asked to complete the Beck Suicide Ideation Scale, the

Beck's Depression Inventory, and the State-Trait Anxiety Inventory. The rates of suicide ideation and depressive and anxiety symptoms between ADHD subjects and normal control subjects were compared using the Chi-squared test (c2 test). All analyses were conducted using SPSS software version 24 (IBM SPSS Institute), and P < 0.05 was considered statistically significant.
Results: There were significant differences between ADHD subjects and normal control subjects in suicide ideation and depressive and anxiety symptoms (P < 0.01). ADHD subjects showed more suicide ideation and depressive and anxiety symptoms compared with normal control subjects. Suicidal ideation was reported by 22.4 percent (11 of 49) of the ADHD group and 3.7 percent (nine of 245) of normal control subjects. Depression was revealed by 44.5 percent (20 of 49) of the ADHD group and 22.0 percent (54 of 245) of normal control subjects. Anxiety was displayed by 24.4 percent (12 of 49) of the ADHD group and 11.8 percent (29 of 245) of normal control subjects.
Conclusions: The symptoms of ADHD might have a significant role in the development of suicide ideation via emotion such as depression and anxiety in school-age youths with ADHD. Appropriate management of ADHD symptoms is needed to reduce suicidal ideation in school-age youths with ADHD

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J Am Acad Child Adolesc Psychiatry. 2017;56:S168.

CLINICAL AND NEUROPSYCHOLOGICAL FACTORS ASSOCIATED WITH TREATMENT RESPONSE AND ADVERSE EFFECT OF ATOMOXETINE IN KOREAN CHILDREN WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER (ADHD).

Kim H-W, Park KJ.

Objectives: The objective of this study was to investigate clinical and neuropsychological factors associated with treatment response and adverse effect of atomoxetine in Korean children with ADHD.
Methods: Children with ADHD were recruited at the Department of Psychiatry of Asan Medical Center, from April 2015 to March 2017. Diagnoses of ADHD and comorbid psychiatric disorders were confirmed with Kiddie Schedule for Affective Disorders and Schizophrenia-Present and Lifetime Version (K-SADS-PL). The participants were treated with atomoxetine for 12 weeks and illness severity were scored using ADHD rating scale (ARS), Clinical Global Impressions - Severity (CGI-S) and/or Clinical Global Impressions -Improvement (CGI-I) at baseline and 12th week. The participants were also evaluated using ATA (Advanced Test of Attention) and KPRC (Korean Personality Rating Scale for Children) at baseline and 12th week. Paired t-test and mixed between-within analysis of variance were used.
Results: Forty-two children with ADHD (age 8.1-1.3 years, 36 boys) were included in this study. Among them, four subjects discontinued treatment before week 12 because of atomoxetine adverse effect (n = 3) and withdrawal of consent (n = 1). Among 38 subjects who completed the 12-week trial, 18 were treatment responders. Commission errors on visual ATA (p = 0.020) and social dysfunction subscale on KPRC (p = 0.043) at baseline were higher in treatment non-responders than in responders. Mood change, including depressed mood, labile affect, irritability, and anger/hostility, were observed in seven subjects among 42 subjects enrolled, and three of them discontinued medication because of mood change. Mood change related to atomoxetine treatment was more frequent in girls (p = 0.004) and intelligence quotient (p = 0.048) was higher in participants with mood change than in those without mood change. Reaction time (p = 0.004) was significantly higher and reaction time variability (p = 0.032) was significantly lower on auditory ATA at baseline in participants with mood change.
Conclusions: Our results provide preliminary evidence that clinical and neuropsychological characteristics could be predictors of treatment response or adverse effect of atomoxetine. Further long-term studies in a larger sample group are needed

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J Am Acad Child Adolesc Psychiatry. 2017;56:S161-S162.

GLUTAMATERGIC NETWORK GENE MUTATION, SUBCORTICAL BRAIN VOLUME, AND PSYCHIATRIC FUNCTIONING IN SUBJECTS WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER (ADHD).

Lugo-Candelas C, Hakonarson H, Squires L, et al.

Objectives: An enrichment in copy number variants (CNVs) in a network of genes impacting glutamatergic signaling and neuronal connectivity (GRM) has been identified in subjects with ADHD. Beyond a diagnosis of ADHD, little is known about the neural and psychiatric phenotype of subjects with GRM CNVs. We examined subcortical brain volume and functioning in subjects with ADHD with and without GRM CNVs and in healthy controls (HC).

Methods: Subcortical brain volume, psychiatric functioning, and genetic data were analyzed in 72 subjects with (n = 39) and without (n = 33) ADHD (mean age = 10.38 ± 3.09 years; 52 males; 20 females). Structural MRI brain scans were analyzed using Freesurfer. This pilot of eight subjects with ADHD were genotyped: seven had GRM CNVs. Psychiatric functioning was assessed via the Child Behavior Checklist.

Results: In line with prior research, subjects with ADHD demonstrated volumetric reductions in the left putamen (p = 0.05), right accumbens (p = 0.05), and left amygdala (p = 0.04), with similar trends in the left hippocampus (p = 0.06), and right caudate (p = 0.09). Subjects with ADHD had increased volume in the left thalamus (p = 0.03) with a trend in the left pallidum (p = 0.09). Post-hoc analyses indicated this increase was driven by subjects with GRM CNVs, who had greater left thalamus and pallidum volumes than the HCs (ps < 0.003), and ADHD subjects without GRM mutations (ps = 0.001). ADHD subjects with GRM CNVs were reported to have more depression, social problems, aggression, and rule-breaking behavior than ADHD subjects without GRM CNVs (ps < 0.02) and HCs (ps < 0.002).

Conclusions: ADHD subjects with GRM CNVs present a distinct profile from those without GRM CNVs, including differences in brain structure and psychiatric symptoms. Metabotropic glutamate receptors are present in the thalamus and have been implicated in psychiatric disorders, yet their role in psychiatric disease is unknown. Preliminary data suggests that within this heterogeneous disorder, subjects with ADHD with GRM mutations may represent a more impaired subsample with a distinct neurobiological profile. Research will need to explore the role of GRM CNVs in the pathophysiology of ADHD

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J Am Acad Child Adolesc Psychiatry. 2017;56:S284-S285.

MEDICATION ADHERENCE MONITORING IN PEDIATRIC AND YOUNG ADULT POPULATIONS ON ATTENTION-DEFICIT/HYPERACTIVITY DISORDER (ADHD) STIMULANT MEDICATIONS.

Ko M.

Objectives: The goals of this presentation are to identify potential nonadherence among pediatric, adolescent, and young adult patients who were prescribed ADHD stimulant medications and assess the differences in illicit substance and/or nonprescribed medication use in patients testing positive versus negative for the ADHD medication.

Methods: Urine samples submitted to the laboratory between 2014 and 2016 from patients (ages 6-25 years inclusive), who were documented on the laboratory requisition to have been prescribed an amphetamine or methylphenidate medication for the treatment of ADHD, were included in the analysis. The first urine sample obtained from each patient was analyzed for the presence of the prescribed ADHD medication, illicit substances [marijuana metabolite (tetrahydrocannabinol, THC) and cocaine metabolite (benzoylecgonine)], and nonprescribed opioid or benzodiazepine medications.

Results: Samples were analyzed from 4,449 patients; 66.4 percent of patients were male, and the mean age was 14.1 5.5 years. Overall, 30.2 percent of patients tested negative for their prescribed ADHD medication. Patients aged 6 to 10 years had the lowest rate of negative test results (21.0%) and patients aged 18 to 21 years had the highest rate [45.5%; adjusted OR (aOR) 3.2 (95% CI 2.5-4.1)]. Illicit substances, primarily THC, were rarely detected for patients under age 14 years but were detected in 11.8, 20.8, and 20.0 percent of patients ages 14 to 17, 18 to 21, and 22 to 25 years, respectively. Detection of nonprescribed opioid medications was rare in patients <18 years of age but were found in 7.7 and 11.4 percent of patients ages 18 to 21 and 22 to 25 years, respectively. Patients who tested negative for prescribed ADHD medication were significantly more likely than patients who tested positive to have THC detected in the urine sample [17.3 vs. 7.1%; aOR 1.9 (95% CI 1.5-2.4)].

Conclusions: Urine drug monitoring in patients prescribed stimulant ADHD medication can be of value both for evaluating adherence to ADHD therapy and identifying the inappropriate use of illicit substances and/or nonprescribed medications. The data suggest that potential nonadherence to prescribed stimulant ADHD therapy is associated with marijuana use and that detection of marijuana in children as young as ages 14 to 17 years is not uncommon

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J Am Acad Child Adolesc Psychiatry. 2017;56:S130.

AACAP ELAINE SCHLOSSER LEWIS AWARD FOR RESEARCH ON ATTENTION-DEFICIT DISORDER CAN WE IMPROVE TREATMENTS FOR ATTENTION-DEFICIT/HYPERACTIVITY DISORDER?

McCracken JT.

Objectives: ADHD represents a prevalent and largely persistent childhood onset disorder. Despite treatments, impairment is common, and disorder course is unchanged. Cognitive deficits represent sources of impairment and persistence. This presentation summarizes research on combination pharmacotherapy aimed at improving clinical and cognitive outcomes in ADHD and whether EEG-based signatures of treatment may yield insight into the mechanisms of combination therapy, possibly representing a biomarker of response.

Methods: A randomized, double-blind, placebo-controlled comparative trial of dexmethylphenidate (DMPH), guanfacine (GUAN), and combination (COMB) enrolling subjects ages 7-14 years with ADHD is described. We examined three primary outcomes: 1) symptomatic benefit; 2) cognitive enhancement; and 3) EEG spectral power changes.

Results: A total of 207 subjects received drug therapy, 182 completed clinical and cognitive assessments, and 179 provided EEGs at baseline and at weeks four and eight. Clinically, a modest, consistent superiority in ADHD-Rating Scale-IV (ADHD-RS-IV)-inattentive symptom scores for COMB versus DMPH ($P = 0.05$) and GUAN ($P = 0.02$) groups was seen, as well as for Clinical Global Impression-Improvement ($P = 0.01$). Cognitive improvement was restricted to working memory, with COMB and DMPH significance versus control subjects ($D = -0.25$ and -0.30), respectively. EEG showed distinct profile by condition, with DMPH and COMB showing increased centroparietal beta and decreased theta; COMB was associated with greater decreases in theta versus DMPH and GUAN.

Conclusions: A combination of DMPH and a-agonist treatment represents a strategy for improved ADHD clinical outcomes, but findings illustrate the challenge of normalizing cognition in ADHD. More research is needed on approaches to address ADHD cognitive deficits, which may yield disordermodifying therapies

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J Am Acad Child Adolesc Psychiatry. 2017;56:S168.

EFFECT OF PHARMACOLOGICAL TREATMENT FOR ATTENTION-DEFICIT/HYPERACTIVITY DISORDER (ADHD) ON MOTOR COORDINATION.

Kim H-W, Joung Y-S, Park KJ.

Objectives: The objective of this study was to investigate the effect of pharmacological treatment for ADHD on motor coordination, using the Developmental Coordination Disorder Questionnaire (DCDQ).

Methods: Participants were recruited from April 2015 to November 2016 from the Department of Psychiatry at Asan Medical Center and were treated for three months with methylphenidate or atomoxetine. Illness severity at baseline and three months were scored using the ADHD-rating scale (ARS), Clinical Global Impressions-Severity (CGI-S), and/or CGI-Improvement (CGI-I). A total of 39 children with ADHD (age 8.0 ± 1.4 years, 36 boys) completed the Advanced Test of Attention (ATA), and parents of children completed DCDQ at baseline and at three months. Paired t-tests mixed between-within analysis of variance and correlation analysis were used.

Results: CGI-S ($P < 0.001$), ARS ($P < 0.001$), and fine motor/handwriting skill ($P = 0.005$) on DCDQ were significantly changed between pre- and posttreatment. The participants were divided into the following groups: 1) those most likely to have developmental coordination disorder (DCD) ($n = 23$; $P < 0.001$); 2) those most likely not to have DCD ($n = 16$; $P < 0.001$); 3) those with control during movement ($P < 0.001$); and 4)

those with fine motor/handwriting skill (P < 0.001). General coordination scores on DCDQ have a main effect on each of these groups. Fine motor/handwriting skill on DCDQ has significant main effect for time [F(1,37) = 7.31, P = 0.010, h2 = 0.405], and interaction effect between group and time was also significant [F(1,37) = 4.63, P = 0.038, h2 = 0.111]. The baseline visual commission error on ATA has significant correlation with changes on DCDQ total scores (r = 0.330, P = 0.040).
Conclusions: Our results provide preliminary evidence that pharmacological treatment for ADHD improves not only core symptom of ADHD but also motor coordination. Further study is needed to confirm the effect of pharmacological treatment for ADHD on motor coordination

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J Am Acad Child Adolesc Psychiatry. 2017;56:S285-S286.
THE STUDY OF COMPUTERIZED EXECUTIVE FUNCTION TRAINING ON CHILDREN WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER (ADHD) IN SHANGHAI.
Li Y, Du Y.
Objectives: The deficits in executive functions (EF) seem to play a role in ADHD. This study focuses on computer-based programs designed to promote executive function training in children with ADHD and to explore whether they improve the deficits in executive functions and clinical behaviors.
Methods: Children with ADHD (n = 56) received computerized executive function training and medication, and the scores of neuropsychological tests and symptom scales at baseline and after 4 weeks of training were evaluated.
Results: After training, there were significant improvements in the main domains of EF tests, including correct number and correct rate in test B of Stroop test (P < 0.001), persistent error response, conceptual level and sustained response scores of the Wisconsin Card Sorting Test (WCST) (P < 0.01), the digit span, coding and symbol search scores of Wechsler Intelligence Scale for Children, Fourth Edition (WISC-IV) (P < 0.05), spatial weights matrix (SWM) errors, interval errors, SWM strategy, Standard Occupational Classification, and scores of CANTAB (P < 0.05). The learning problems and hyperactive index scores of the patient satisfaction questionnaire (PSQ) were decreased significantly (P < 0.05). At the end of 4 weeks of treatment with atomoxetine, children showed improvement in the correct rate in test B of Stroop test, conceptual level and sustained response scores of WCST, the digit span scores (P < 0.05), and coding and symbol search scores (P < 0.01) of WISC-IV; their scores in SWM, total interval errors, and SWM strategy were reduced significantly (P < 0.05). In the PSQ questionnaire, the scores of behavior problems, learning problems, hyperactivity impulsivity, hyperactivity index, and anxiety (P < 0.05) were decreased significantly.
Conclusions: Through the exploratory research, we found that computerbased training could improve the executive function performance on response inhibition, working memory, processing speed, cognitive flexibility, and plan-monitoring fields in children with ADHD, as well as the core symptoms of ADHD

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J Am Acad Child Adolesc Psychiatry. 2017;56:S284.
ROBOT MOTION TRACKING ANALYSIS IN ATTENTION-DEFICIT/HYPERACTIVITY DISORDER (ADHD).
Kim K, Min A, Ahn D.
Objectives: ADHD is a neurodevelopmental disorder characterized by hyperactivity, inattention, and impulsivity. Before 1980, the disease was named attention-deficit disorder (ADD) and then changed to ADHD, with an emphasis on the importance of hyperactivity symptoms. Nonetheless, there are limits to measuring objective activity because the assessments are largely based on observations of therapists and caregivers.
Methods: The participants evaluated in this study were 35 children diagnosed with ADHD and 50 typical development children within the age range of 5 to 12 years. The purpose of this study was to examine behavioral levels using the robot motion-tracking system and to conduct an evaluation and comparative analysis of the results from the Child Behavior Checklist (CBCL) and the Attention-Deficit/Hyperactivity Disorder Diagnostic Scale (ADHD-DS), which are the current standard evaluations for ADHD diagnosis.

Results: There were significant average differences between the ADHD group and normal group in attention problems (52.78 3.90 vs. 63.40 7.57, P < 0.001) and ADHD problems (53.64 5.31 vs. 67.77 11.07, P < 0.001) according to the results of the CBCL and the ADHD-DS (25.37 6.30 vs. 12.36 3.39, P < 0.001). There were also significant differences between the movement distance (4,968.64 4,201.53 vs. 830.89 6,324.45, P < 0.001) and movement speed (361.17 133.49 vs. 735.60 1,227.55, P = 0.035) in that the typical developmental group traveled long distances more slowly, whereas the ADHD group traveled short distances more quickly. The results of correlation analysis showed that distance of travel was significantly correlated with attention problems (according to the CBCL) and ADHD problems (according to CBCL and ADHD-DS), whereas movement speed was significantly correlated with the ADHD problems according to the CBCL and ADHD-DS.
Conclusions: The children with ADHD were characterized by moving small distances faster than children without ADHD, within the same period of time during the tasks. Moreover, the robot motion-tracking analysis can be used to overcome limitations of previous questionnaires by producing objective information on the children's activities to determine the effectiveness of diagnosis and treatment

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J Am Acad Child Adolesc Psychiatry. 2017;56:S285.

EXECUTIVE FUNCTION DEFICITS IN BOYS WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER (ADHD) CONTRIBUTE TO PARENTING STRESS.

Li M, Du Y, Li Y, et al.

Objectives: We explored the relationship between heterogeneous executive function (EF) deficits and parenting stress among children with ADHD.
Methods: Data from 104 drug-na+»ve boys diagnosed with ADHD (mean age = 9.95 years) and 47 boys showing typical development (mean age = 10.79 years) were collected. Neuropsychological test batteries were used to assess various aspects of EF (inhibition, working memory, planning, and shifting), whereas the Parenting Stress Index (PSI), SNAP-IV, and Behavior Rating Inventory of Executive Function (BRIEF) were used for the parents. Children with EF deficits or intact EF were grouped by confirmatory factor analysis, and twostep clustering, Pearson correlations, and stepwise regression analyses were used afterward.
Results: Inhibition was found to be positively correlated with distractibility/hyperactivity, demandingness, acceptability, parent domain total, and total stress scores on the PSI among boys with ADHD and EF deficits (P < 0.05). Among boys with ADHD but intact EF, planning was correlated positively with the reinforces parent and attachment subscales of the PSI, whereas working memory was correlated with the reinforces parent subscale only (P < 0.05). Inhibition was an independent predictor of demandingness among boys with ADHD and EF deficits, whereas planning was a predictor of attachment among boys with ADHD and intact EF. Furthermore, planning and inattention symptoms together predicted the reinforces parent subscale of the child domain.
Conclusions: Overall, we found relationships between EFs and various domains of parenting stress according to the presence or absence of EF deficits among children with ADHD. The underlying mechanisms of these associations remain to be clarified

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J Am Acad Child Adolesc Psychiatry. 2017;56:S159.

CATEGORICAL AND DIMENSIONAL ASSESSMENT OF NUCLEUS ACCUMBENS AND AMYGDALA CONNECTIVITY IN DISRUPTIVE BEHAVIOR DISORDERS AND ATTENTION-DEFICIT/HYPERACTIVITY DISORDER (ADHD).

Costa Dias TG, Sato JR, Fair DA, et al.

Objectives: Previous studies support the involvement of reward and emotional regions [e.g. nucleus accumbens (NAcc), and amygdala (Amyg)] in disruptive behavior disorders (DBD) and ADHD. We investigated functional connectivity of NAcc and Amyg in youth with ADHD or DBD, and control subjects, and the correlation between functional connectivity and behavior dimensions.
Methods: We collected resting-state fMRI data for children (mean age = 11.28 years) with ADHD (n = 25), DBD (n = 22), and controls (n = 236) in two Brazilian sites, using 1.5 Tesla scanners and the same

parameters. We performed seed-based analysis, with NAcc and Amyg as seeds, and compared the groups (DBD, ADHD, controls) for the NAcc and Amyg functional connectivity. We also correlated NAcc and Amyg functional connectivity with Child Behavior Checklist (CBCL) scores of attention problems, aggressive behavior, and rule-breaking behavior. Analyses were controlled for: 1) site; 2) age; 3) sex; and 4) scan remaining time (after removing volumes due to excess movement). Monte Carlo simulation was implemented to correct for multiple comparisons ($p < 0.05$; $z > 3.00$).
Results: DBD and ADHD groups did not differ from controls for the NAcc, but DBD showed weaker connectivity with posterior insula, compared to ADHD. Controls and DBD were not significantly different in the Amyg connectivity. Subjects with ADHDshowed atypical Amyg connectivity with: 1) visual cortex; 2) precentral gyrus; and 3) inferior parietal lobule. Subjects with ADHD, compared to DBD, showed weaker Amyg functional connectivity with visual cortex. Inattention and aggression scores were associated with NAcc connectivity to fusiform gyrus and dorsomedial prefrontal cortex. Inattention was correlated with Amyg connectivity to inferior parietal lobule, middle temporal gyrus, and superior precentral sulcus. Aggression was related with Amyg connectivity to precuneus and superior frontal gyrus. Rule-breaking scores were correlated with NAcc-superior frontal gyrus connectivity, and with Amyg connectivity to posterior cingulate cortex, precuneus, medial prefrontal cortex, and lingual gyrus.
Conclusions: Our results suggest that the traditional categorical approach is not sufficient to characterize the NAcc and Amyg functional connectivity in DBD and ADHD, and propose that a dimensional approach may contribute to better examine DBD and ADHD neurobiology

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J Am Acad Child Adolesc Psychiatry. 2017;56:S77.

DEPRESSIVE DISORDERS IN ADOLESCENTS WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER: STRATEGIES FOR ASSESSMENT AND TREATMENT.

Daviss WB.

Objectives: Participants will learn practical and empirically supported strategies when available for accurately assessing depressive disorders among their moody patients with ADHD. Participants will also learn ways to improve their pharmacological and psychosocial treatments of such comorbid problems in their patients with ADHD.
Methods: Dr. Daviss will review the potential risk factors and strategies for assessing comorbid depression in patients with ADHD. He will also summarize the literature that supports pharmacological and psychosocial treatments for comorbid depression, including recommendations from a consensus panel of experts. Case presentations, handouts, and other potentially helpful materials, such as rating scales and treatment algorithms, will be provided to participants and reviewed during the presentation.
Results: Through this presentation and group discussion spurred by it, participants will improve their working knowledge of how to assess and treat such depressive disorders occurring in youth with ADHD.
Conclusions: Ultimately, participants will be more informed on how to diagnose and treat patients with ADHD who have comorbid mood problems in their clinical practice and identify continuing knowledge gaps in our field that necessitate further research

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J Am Acad Child Adolesc Psychiatry. 2017;56:S278-S279.

EARLY-ONSET EFFICACY AND SAFETY PILOT STUDY OF AMPHETAMINE EXTENDED-RELEASE ORAL SUSPENSION IN THE TREATMENT OF CHILDREN WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER (ADHD).

Childress A, Berry S, Pardo A, et al.

Objectives: The goal of this session is to assess the efficacy and safety of amphetamine extended-release oral suspension (AMPH EROS) in reducing the symptoms of ADHD compared with placebo in children with ADHD. This double-blind (DB), randomized, two-period, two-treatment, two-sequence, crossover study was designed primarily to test the onset of action of AMPH EROS as early as 30 minutes postdose.
Methods: Male and female children (aged 6-12 years) diagnosed with ADHD and with an ADHD-Rating Scale-5 (ADHD-RS-5) score at screening 90th percentile for sex and age were enrolled in the study. A daily

dose between 5 and 20 mg of AMPH EROS was determined for each subject during an open-label phase by the investigator and was based on history of medication treatment, adequate symptom control, and tolerability. Subjects were randomized to receive either AMPH EROS or placebo in a DB laboratory classroom session and then crossed over to receive the opposite treatment in a second classroom session six days later. Dosing in the DB phase was fixed at 15, 17.5, or 20 mg. Drug efficacy was assessed before dosing and at 30 minutes and 3 hours after dose using the Swanson, Kotkin, Agler, M-Flynn, and Pelham (SKAMP) rating scale. Safety was assessed measuring vital signs and adverse events.
Results: At 30 minutes and 3 hours after dose, the change from predose SKAMP-Combined scores for AMPH EROS compared with placebo were statistically significant, with 8.6 and 17.2 points difference in the SKAMPCombined score (P = 0.01, P = 0.0002), respectively. The effect sizes for AMPH EROS at the time points of 30 minute and 3 hours postdose were 0.95 and 1.57, respectively. Adverse events (>10%) reported during the open-label phase included upper respiratory tract infection, fatigue, abdominal pain upper, headache, decreased appetite, and affect lability.
Conclusions: AMPH EROS was effective in reducing symptoms of ADHD at 30 minutes and 3 hours postdose. Adverse effects reported were mild or moderate in severity and consistent with those of other extended-release amphetamines

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J Am Acad Child Adolesc Psychiatry. 2017;56:S286.

ATYPICAL FUNCTIONAL CONNECTIVITY IN ADOLESCENTS AND ADULTS WITH PERSISTENT AND REMITTED ATTENTION-DEFICIT/HYPERACTIVITY DISORDER (ADHD).

Michelini G, Jurgiel J, Bakolis I, et al.

Objectives: ADHD diagnosed in childhood often persists into adolescence and adulthood, but the neural mechanisms underlying ADHD persistence/remission are poorly understood. In a follow-up study, we aimed to examine whether brain functional connectivity, measuring the interdependency of brain oscillations between brain regions, reflects enduring deficits unrelated to ADHD outcome or is a marker of ADHD remission, improving concurrently with clinical profiles.
Methods: On average, six years after assessments in childhood, high-density EEG was recorded in 110 adolescents and young adults with childhood ADHD (87 persisters, 23 remitters) and 169 typically developing control subjects during an arrow-flanker task-eliciting cognitive control. Functional connectivity was quantified by applying a network-based (graph-theory) approach. Groups were compared on connectivity metrics in theta, alpha, and beta frequency bands in incongruent (high-conflict) trials before target onset (prestimulus), during target processing (poststimulus), and in the degree of change from prestimulus to poststimulus. ADHD outcome was examined with clinical diagnosis (persistent/remitted ADHD) and with ADHD severity indicated by continuous measures of symptoms and functional impairment.
Results: ADHD persisters showed increased prestimulus connectivity in theta, alpha, and beta oscillations; increased poststimulus beta connectivity; and reduced prestimulus/post-stimulus change in theta connectivity compared with control subjects (all P < 0.01). In most measures showing ADHD persistercontrol differences, ADHD remitters differed from control subjects (all P < 0.05) but not from persisters. Likewise, no association emerged between connectivity measures and ADHD severity in participants with childhood ADHD.
Conclusions: Adolescents and young adults with persistent and remitted ADHD shared atypical connectivity profiles (hyperconnectivity and reduced ability to modulate connectivity patterns with task demands), compared with control subjects. These results indicate that these connectivity impairments may represent enduring deficits in individuals with childhood ADHD, irrespective of current diagnostic status in adolescence/young adulthood

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J Am Acad Child Adolesc Psychiatry. 2017;56:S285.

INDIVIDUAL COGNITIVE SUBTYPE STATUS CAN BE PREDICTED IN YOUTH WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER (ADHD).

Leikauf J, Sacchet MD, Griffiths K, et al.

Objectives: We previously reported a first attempt to identify objectivelydefined subtypes of youth with ADHD: neurocognitively-defined ADHD subgroups (putative biotypes) using unsupervised machine learning. Here, we aimed to determine whether these subtypes could be independently replicated in novel test datasets, and whether a predictive model could be generated that accurately predicts group membership at the individual level.

Methods: We utilized data from two independent studies (n = 336 and n = 170) to determine whether previously identified (n = 140) cognitive subtypes could be independently replicated in these larger datasets. All studies included participants aged 6-17 years. We used a previously validated, computerized cognitive battery that was identical across studies. Hierarchical clustering was used to generate clusters/subtypes. Support vector machines were trained and used to form a predictive model, then applied to the smaller (test) datasets. Individual predicted group membership in the test datasets were compared to actual groups identified independently by hierarchical clustering to generate accuracy statistics and statistically tested using the binomial test.

Results: Average accuracy in cross-validated testing was 84 percent ($p < 0.001$). Accuracy in the n = 170 test set was 80 percent ($p < 0.001$). In the previously reported data, balanced accuracy was 71 percent ($p = 0.014$). Cognitive subtypes were similar to those previously identified in their patterns of deficits: a cognitively inattentive group with long and variable reaction times on sustained attention tasks and a cognitively impulsive group with poor performance across task scores measuring inhibition.

Conclusions: Previously identified cognitive biotypes were independently identified in two novel datasets, in a total of 646 youth with ADHD. An independently generated predictive model significantly predicted an individual's type in each of the separate datasets. Cognitively inattentive and cognitively impulsive types are replicable and individual cognitive subtype status can be predicted with good accuracy using cognitive markers

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J Am Acad Child Adolesc Psychiatry. 2017;56:S334-S335.

SUBSTANCE USE AMONG CHILDREN WITH AND WITHOUT ATTENTION-DEFICIT/HYPERACTIVITY DISORDER FOLLOWED PROSPECTIVELY INTO EARLY ADULTHOOD IN THE MTA.

Mitchell JT, Howard AL, Swanson JM, et al.

Objectives: ADHD is a risk factor for substance abuse. However, few studies have prospectively examined substance use, as opposed to disorder, from childhood-diagnosed ADHD into adulthood. The current report uses the Multimodal Treatment Study (MTA) of children with ADHD, a longitudinal dataset with methodological strengths to clarify the extent to which ADHD elevates substance use risk through early adulthood. We hypothesized the following. 1) Childhood ADHD will predict elevated substance use frequency in early adulthood; 2) a greater percentage of adolescents from the ADHD group than the non-ADHD group will engage in developmentally atypical levels of substance use before adulthood that will promote increased substance use in adulthood; and 3) substance use will escalate more rapidly in the ADHD group than the non-ADHD group among developmentally atypical early substance users.

Methods: Children diagnosed with ADHD (ages 7-9 years; N = 547) and an age- and sex-matched local normative comparison group (LNCG; N = 258) participated in the MTA. Substance use was assessed approximately every two years from mean age of 10 years to the mean age of 25 years, with retention rates >80 percent.

Results: A greater proportion of the ADHD group were weekly marijuana users (32.8% ADHD, 21.3% LNCG; P = 0.002) and smoked tobacco daily (35.9% ADHD, 17.5% LNCG; P < 0.0001) by early adulthood. No group differences emerged for alcohol use, nonmarijuana illicit drug use, or prescription drug (i.e., stimulant) misuse. Substance use escalated into adolescence and declined slightly after age 21 years in both groups. The ADHD group had greater increases in heavy drinking (P = 0.009) and illicit drug use (P = 0.034) through age 21 years, which were no longer significant by age 25 years. In contrast, both groups had similar rates of increases in marijuana and tobacco use through age 21 years but higher rates in the ADHD group by age 25

years (P = 0.074 marijuana, P < 0.0001 tobacco). Substance use escalation rate did not differ between groups for developmentally atypical early users.
Conclusions: Children with ADHD are at increased risk for marijuana and tobacco use into young adulthood. Prescribed and illicit stimulant misuse did not differ and was low (<2%). Substance-specific escalation in the ADHD group highlights the need for preventative interventions

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J Am Acad Child Adolesc Psychiatry. 2017;56:S265.

DOUBLE-BLIND SHAM-CONTROLLED PILOT STUDY OF TRIGEMINAL NERVE STIMULATION (TNS) FOR ATTENTION-DEFICIT/HYPERACTIVITY DISORDER (ADHD).

McGough JJ, Loo SK, Cowen J, et al.

Objectives: Trigeminal nerve stimulation (TNS), a minimal risk, noninvasive method of neuromodulation, has proven effective in treatment-refractory depression and epilepsy and is associated with increased activation in the anterior cingulate gyrus on positron emission tomography (PET) imaging. A previous open-label investigation suggested potential benefits of TNS in treating ADHD, but was neither controlled nor conducted in blinded fashion. This double-blind, sham-controlled study is the first blinded controlled study of TNS in youth and first to examine the efficacy of TNS as an ADHD treatment.
Methods: Children aged 8-12 years, with minimal full scale IQ=85, and diagnosed with ADHD via the Kiddie Schedule for Affective Disorders and Schizophrenia (KSADS), were randomized to four weeks of nightly treatment with active or sham TNS. In the active TNS group, low-grade electrical stimulation was generated during sleep by a small device worn on the participant's shirt and administered via an electrode patch applied to the forehead each night at bedtime. Active versus sham treatments were identical except that no stimulation was administered in the sham group. Assessments included weekly clinician administered parent ADHD-rating scales (ADHD-RS), Clinical Global Impression (CGI) severity and improvement scales, and parent- and teacher-completed Conners' ratings scales. Cognitive testing and EEG were conducted at selected visits.
Results: The sample group of the study included 62 participants. ADHD-RS scores trended towards significant improvement in the active group (time effect: F = 23.37, df = 4/223, p < 0.001; group effect: F = 3.46, df = 1/60, p = 0.07; group x time interaction: F = 2.21, df = 4/223, p = 0.07). At final visit based on ADHD-RS scores, Cohen's D estimate = 0.5, suggesting a medium effect size. CGI-Improvement scores favored active treatment (X2 = 8.50, df= 1, p = 0.004). There were no significant differences in weight, height, pulse, or blood pressure. There were no clinically meaningful adverse events in either condition.
Conclusions: Although limited by a small sample size and short-term duration, this study demonstrated potential efficacy of TNS as an ADHD therapy and provides further evidence that TNS is safe and of minimal risk in children. Ongoing analyses will examine potential effects of TNS on cognition, brain activation, and neural circuitry. Future research is needed to assess the durability of treatment response and impact on brain development with sustained use

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J Am Acad Child Adolesc Psychiatry. 2017;56:S334.

ADULT FOLLOW-UP OF THE MULTIMODAL TREATMENT STUDY OF ATTENTION-DEFICIT/HYPERACTIVITY DISORDER (MTA): PARTICIPANTS' SUBSTANCE USE AND GROWTH TRAJECTORIES.

Hechtman L, Wilens TE.

Objectives: The objective of this symposium is to present new findings in adulthood from the multimodal treatment study on ADHD that pertains to substance use and growth trajectories.
Methods: The Multimodal Treatment Study of Attention-Deficit/Hyperactivity Disorder started as a 14-month randomized clinical trial with 579 children (aged 7-10 years) and 258 age- and sex-matched classmates (local normative comparison group, LNCG) and proceeded as a naturalistic follow-up with assessments in childhood, adolescence, and adulthood (mean age 25 years). Dr. Greenhill will present on growth trajectories, height, weight, and body mass index from each assessment point and describe how they related to self-selected, communitybased medication use in consistently, negligibly, and inconsistently medicated

participants. Dr. Mitchell will present new substance use (SU) data for individuals with and without childhood ADHD who were followed prospectively into adulthood. Dr. Swanson will present on the subsample group selected for the Qualitative Interview Study-specifically, how the individuals were selected with regard to persistence and nonpersistence of SU, demographics, effect of stimulant medication use, and ADHD persisters versus desisters. Dr. Jensen will present data fromthe qualitative interviewson turningpoints in the lives of youths with and without ADHD and whether they are linked to SU.

Results: Important findings include the following: 1) increased growth suppression in subjects with ADHD treated early and consistently with stimulant medication compared with those who were treated intermittently or negligibly; 2) a greater proportion of the ADHD group comprised weekly marijuana users and daily tobacco smokers compared with control subjects, but there were no group differences for alcohol or other SU; 3) persistent substance users differed from the nonpersistent substance users, but there were no differences between the ADHD group and LNCG and no effect of stimulant treatment on substance use; and 4) subjects in LNCG reported significantly more reasons for abstaining or stopping substance use. Abstainers, desisters, and persisters of substance use differed in perceptions with regard to positive and negative effects of drugs, level of support, positive turning points, and self-efficacy.

Conclusions: These presentations provide new data on growth trajectories and stimulant medication treatment, as well as greater insight regarding factors contributing to substance use for subjects from the ADHD group and LNCG

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J Am Acad Child Adolesc Psychiatry. 2017;56:S170.

CLINICALLY MEANINGFUL IMPROVEMENTS WITH DR/ER-MPH IN AT-HOME FUNCTIONAL IMPAIRMENT DURING THE EARLY MORNING, LATE AFTERNOON, AND EVENING IN CHILDREN WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER (ADHD).

Wilens TE, Faraone SV, Hammerness P, et al.

Objectives: The efficacy and safety of DR/ER-MPH, a delayed-release and extended-release methylphenidate, were evaluated in a phase 3 trial of children with ADHD. In addition to improving ADHD symptoms, DR/ER-MPH demonstrated statistically significant reductions in at-home functional impairment versus placebo (PBO); however, it is unknown if these improvements are clinically relevant. This post hoc analysis evaluated the clinical meaningfulness of DR/ER-MPH versus PBO in improving at-home functional impairment.

Methods: Data were analyzed from a randomized, double-blind, multicenter, PBO-controlled, phase three trial of HLD200 in children (aged 6-12 years) with ADHD (NCT02520388). At-home early morning functional impairment was assessed by the Before School Functioning Questionnaire (BSFQ) and Parent Rating of Evening and Morning Behaviors-Revised (PREMB-R) morning (AM) subscale. At-home late afternoon/evening functional impairment was assessed by the PREMB-R evening (PM) subscale. Clinically meaningful improvements were defined using anchor-based estimates with Clinical Global Impression-Improvement (CGI-I) scores of 1 (very much improved) and 2 (much improved) as anchors. Cumulative percentages of children with changes from baseline in BSFQ, PREMB-R AM, and PREMB-R PM anchored to CGI-I were assessed.

Results: Using CGI-I scores of 1 and 2 as anchors, reductions in BSFQ of 27 and 20, PREMB-R AM of five and three, and PREMB-R PM of nine and five were defined as clinically meaningful. After three weeks of treatment, a higher proportion of children treated with DR/ER-MPH versus PBO demonstrated a much or very much improved (CGI-I -¦ 2) change from baseline in BSFQ (65.4% vs 43.3%; P = 0.012), PREMB-R AM (73.4% vs 41.3%; P < 0.001), and PREMB-R PM (64.6% vs 42.7%; P = 0.01). Similarly, a higher proportion of children treated with DR/ER-MPH versus PBO demonstrated very much improved (CGI-I = 1) change from baseline in BSFQ (51.3% vs 23.9%; P = 0.001), PREMB-R AM (45.6% vs 24.0%; P = 0.008), and PREMB-R PM (46.8% vs 24.0%; P = 0.005).

Conclusions: Clinically meaningful and statistically significant improvements in at-home functional impairment from the early morning until evening were achieved as shown by multiple validated rating scales in children with ADHD treated with DR/ER-MPH for three weeks

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J Am Acad Child Adolesc Psychiatry. 2017;56:S288-S289.

POPULATION PHARMACOKINETICPHARMACODYNAMIC MODELING OF A NOVEL METHYLPHENIDATE EXTENDED-RELEASE ORALLY DISINTEGRATING TABLET IN PEDIATRIC PATIENTS WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.

Teuscher N, Sikes C, McMahen R, et al.

Objectives: A methylphenidate (MPH) extended-release oral disintegrating tablet (MPH XR-ODT) has recently been developed. This analysis sought to develop a population pharmacokinetic- (PK) pharmacodynamic (PD) model to describe the PD response data in an ADHD pediatric classroom study of MPH XR-ODT and to simulate the PD responses for pediatric patients across a range of body weights and MPH XR-ODT doses.

Methods: The PK-PD model was based on data from a phase 3, randomized, controlled laboratory classroom study in pediatric patients with ADHD and a previously established pediatric PK model. The classroom study evaluated the efficacy of MPH XR-ODT using the Swanson, Kotkin, Agler, M-Flynn, and Pelham Scale (SKAMP) combined score. The PK model was a two input, one compartment, first order elimination model with body weight as a covariate on clearance and volume of distribution. The model was used to simulate maximum reduction in the SKAMP combined scores and SKAMP combined scores across a range of body weights (7-100 kg) and dose levels [equivalent to 10-60 mg MPH hydrochloride (HCl)].

Results: The maximal reduction in SKAMP combined score was approximately 38 units, and the MPH concentration required to achieve 50 percent of the maximal reduction was 14.24 ng/mL, suggesting favorable efficacy for MPH XR-ODT. Model simulation suggested that patients with higher body weights required larger doses of MPH XR-ODT for symptom control. For patients with body weights ranging from 26 pounds to 218 pounds, the optimal MPH XR-ODT doses were 10-60 mg in terms of MPH HCl. A favorable safety profile for MPH XR-ODT may be anticipated because of the lack of discontinuations due to adverse events in either study.

Conclusions: There was a direct correlation between the dose of MPH XRODT required for symptom control and patient body weight. Given that data on the PK-PD relationship for ADHD medications are limited, using the PK-PD model to predict the optimized dose for individual pediatric patients can minimize the lengthy dose titration process and provide insight into a target dose

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J Am Acad Child Adolesc Psychiatry. 2017;56:S233-S234.

NEUROPSYCHOLOGICAL PROFILE DIFFERENCES BETWEEN CHILDREN WITH DISRUPTIVE MOOD DYSREGULATION DISORDER (DMDD) AND ATTENTION-DEFICIT/HYPERACTIVITY DISORDER (ADHD): A PRELIMINARY STUDY.

Taskiran S, Mutluer T, Necef I.

Objectives: Disruptive mood dysregulation disorder (DMDD), characterized by severe irritability, and ADHD are highly comorbid. Clinical observation suggests that patients with DMDD have greater impairment in functioning at school. We compared the neuropsychological assessment scores across three groups of participants to test whether any cognitive differences exist among children with ADHD, DMDD and healthy control (HC) subjects.

Methods: The study sample group consisted of 43 participants (14 DMDD, 14 ADHD and 15 age-matched HC, mean age = 9.51; SD = 2.10). All the subjects diagnosed with DMDD had comorbid ADHD. Subjects underwent extensive diagnostic measures including Kiddie Schedule for Affective Disorders and Schizophrenia (K-SADS). We applied the following tests: trail making test (TMT), symbol cancellation task (SCT), single letter cancellation task (SLCT), digit span learning (DSL), benton judgment of line orientation (JLO), Rey-Osterrieth complex figure test (CFT), letter and symbol cancellation test (LCT, SCT), Stroop color word (TBAG), and Wisconsin card sorting test (WCST).

Results: There were statistically significant differences between these three groups on the TMS, $F(2,41) = 5.270$, $p = 0.009$, structured SLCT, $F(2,41) = 3.376$, $p = 0.044$, unstructured SLCT, $F(2,41) = 5.142$, $p = 0.010$, unstructured SCT, $F(2,41) = 5.282$, $p = 0.009$, the ROCFT, $F(2,40) = 6.622$, $p = 0.003$, the ROCFT: delayed recall condition score, $F(2,40) = 3.647$, $p = 0.035$), the ROCFT: delayed condition time, $F(2,40) = 9.195$, $p = 0.001$), Stroop test: incongruent color words condition, $F(2,40) = 4.522$, $p = 0.017$), Stroop test: naming the color of random words condition, $F(2,40) = 3.647$, $p = 0.035$). Post hoc analyses revealed little difference between ADHD and ADHD and DMDD groups except for the TMT.

Conclusions: Neuropsychological properties for children with DMDD are very similar to those of ADHD. Selective and sustained attentional impairment, working memory, and set shifting difficulties are prominent in both ADHD and DMDD. Although results did not yield a significant difference, we observed more impaired performance in all tests, likely due to greater impulsivity and poorer frustration tolerance. Larger sample size is required to confirm this notion

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J Am Acad Child Adolesc Psychiatry. 2017;56:S253.

CORTICAL EXCITABILITY AND BEHAVIORAL CORRELATES OF COMORBID ADHD IN YOUTH WITH AUTISM SPECTRUM DISORDERS.

Pedapati E, Mooney L, Wu S, et al.

Objectives: The neurological correlates distinguishing youth with autism spectrum disorder (ASD) and youth with ASD and co-occurring ADHD (ASD+ADHD) is poorly understood, despite evidence that ASD+ADHD have higher rates of hospitalization, psychopharmacology, and behavioral concerns than ASD alone.
Methods: Paired pulse transcranial magnetic stimulation (ppTMS) data and relevant behavioral measures were performed based on standard methods from an age and gender matched sample of ASD and ASD+ADHD. These data are baseline measures from recently completed randomized controlled, single dose methylphenidate study in youth with ADHD+ASD.
Results: Twenty-four ASD+ADHD subjects (mean age = 14.5) and 15 ASD only subjects (mean age = 15.1) were included in this analysis. As expected, Conners-3 Parent Rating Scale-Inattention (CPRS-IA), Hyperactivity (CPRS-H), and Executive Functioning (CPRS-EF) scores were significantly higher for the ASD+ADHD group relative to the ASD group. ASD subjects demonstrated significantly enhanced intracortical facilitation (ICF) ($M = 1.26$, $SD = 0.28$, $n = 15$) compared to ASD+ADHD subjects ($M = 1.01$, $SD = 0.22$, $n = 24$; $t = 2.6$, $df = 37$, $p = 0.01$). ICF was significantly inversely correlated with CPRS-EF ($r = -0.350$; $p = 0.029$), CPRS-IA ($r = -0.394$; $p = 0.013$) but not CPRS-H ($r = -0.083$; $p = 0.61$). ICF also correlated with the ADHD-IV Rating Scale (ADHDRS) Inattention scale ($r = -0.432$; $p = 0.007$) but not ADHDRS Hyperactivity scale.
Conclusions: These data suggest that ICF, a rapidly obtained ppTMS measure which is associated with glutamergic activity, is disturbed in ASD+ADHD. ICF is also associated with clinical variables representing the severity of inattention and executive function in ADHD. Further results are expected from the larger RCT which will clarify the impact of methylphenidate on these TMS measures, but also resting state electroencephalography and high-speed eye tracking

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J Am Acad Child Adolesc Psychiatry. 2017;56:S302.

EVALUATING ATTENTION-DEFICIT/HYPERACTIVITY DISORDER DIAGNOSTIC TOOLS IN YOUTH WITH AUTISM SPECTRUM DISORDER.

Yerys B.

Objectives: It is only with the release of the fifth edition of our diagnostic manual (DSM-5) that an individual may carry a diagnosis of both autism spectrum disorder (ASD) and ADHD. Many in the field of ASD have been applying ADHD diagnostic tools to sample groups with ASD without considering whether these tools would be valid in an ASD population. We examined the validity of ADHD diagnostic tools in youth with ASD.
Methods: We collected parent ($n = 386$) and teacher ratings ($n = 203$) on the ADHD Rating Scale, 4th Edition (ADHD-RS-IV) for youth ages 7-17 years with ASD, as well as parent ratings on executive function (Behavior Rating Inventory of Executive Function; $n = 365$). For 22 children in our sample group, we also assessed convergent validity by conducting a well-validated psychiatric interview [Kiddie-Schedule for Affective Disorders and Schizophrenia- Present and Lifetime Version (K-SADS-PL)].
Results: The ADHD-RS-IV showed similar prevalence of ADHD in ASD compared with other large-scale studies using the DSM-based diagnostic tools. The ADHD-RS-IV demonstrated similar relationships with age and parent-reported executive function as is seen in those with ADHD. Furthermore, our exploratory subsample group with a psychiatric interview shows generally good convergence with the ADHD-RS-IV. Whereas the overall factor structure of the scale generally coheres to the expected two-factor solution

(inattention and hyperactivity/impulsivity), the ADHD-RS-IV fails to meet goodness-of-fit criteria for factorial validity.
Conclusions: The present study takes a critical step toward improving the measurement of ADHD symptoms in ASD. We demonstrate that ADHD screeners that closely adhere to DSM descriptions of symptoms will yield expected relationships; however, the failure to achieve factorial validity means that the scale does not adequately separate the constructs of inattention and hyperactivity/impulsivity. This work has implications for the study of ADHD in ASD, and for best practices in the clinic

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J Am Acad Child Adolesc Psychiatry. 2017;56:S286.
AN INVESTIGATION INTO THE UTILITY AND SENSITIVITY OF THE SNAP-IV PARENT- AND TEACHER-RATED QUESTIONNAIRE IN THE ASSESSMENT OF ATTENTION-DEFICIT/HYPERACTIVITY DISORDER (ADHD).
Oxley CJ, Phillips J, Moghraby OS.
Objectives: The purpose of this study is to establish the utility and sensitivity of the Swanson, Nolan and Pelham Teacher and Parent Rating Scale (SNAP-IV) in assessing ADHD in a clinical sample.
Methods: This study consisted of a retrospective review of medical records from a clinical patient sample (N = 65), aged seven to 17 years. Sensitivity of SNAP-IV scores to medication changes were assessed using a two-tailed paired t-test while Cohen's kappa coefficient was used to assess concurrent validity between SNAP-IV and Strengths and Difficulties Questionnaire (SDQ) scores and interrater reliability (parents and teachers). Internal consistency was measured using Cronbach's alpha coefficient. Statistical analysis was performed on the total SNAP-IV scores, both inclusive (items 1 - 26) and exclusive (items 1 - 18) of the ODD items, and across the respective subdomains of inattention, hyperactivity/impulsivity, and ODD.
Results: Total SNAP-IV scores showed no significant change following a medication increase. Significant changes were observed in SNAP-IV scores in the inattentive domain in patients who had no history of medication resistance. SNAP-IV demonstrated acceptable test-retest reliability (a = 0.781) and moderate correlation between parent and teacher ratings (l = 0.626). Correlation between SDQ and SNAP-IV reports was fair for parents (l = 0.256) and teachers (l = 0.286).
Conclusions: This study provides evidence that SNAP-IV can be a reliable and valid screening tool as a component in assessment of ADHD behaviors within a clinical sample. Further research with a larger sample size is required to further test the sensitivity of SNAP-IV to changes in medication dose

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J Am Acad Child Adolesc Psychiatry. 2017;56:S328.
NEUROIMAGING OF CHILDREN WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER WITH AND WITHOUT AGGRESSION.
Pliszka SR.
Objectives: ADHD is often comorbid with disruptive behavior, most commonly reactive forms of aggression. Indeed, approximately half of children with ADHD meet criteria for disruptive behavior disorders (DBDs), such as oppositional defiant disorder (ODD) or conduct disorder (CD). Understanding the neural pathways that predispose children with ADHD to aggression is an important first step in tailoring intervention for these populations. Although many studies have attempted to characterize the neuroanatomical/functional correlates of DBDs, few studies have directly compared youth with ADHD youth with and without clinical significant aggression.
Methods: In the current study, we compared children with ADHD who did not exhibit significant aggression (ADHD-) with those with significant overt displays of aggression (ADHD+). All children completed a high-resolution anatomical scan and an eight-minute resting state functional scan, and completed a semistructured clinical interview with a psychologist or psychiatrist. Regional differences in brain morphology were compared, and differences in resting state connectivity were examined.
Results: As expected, relative to the ADHD(-) group, the ADHD(+) group exhibited significantly greater symptoms of ODD and CD (t-score > 4.43, P < 0.01), but the two groups did not differ in ADHD symptoms endorsed (t-score = 0.99, not significant). The ADHD(+) group had significantly less gray matter volume within the insula and caudate, extending to the orbitofrontal cortex. Preliminary resting state connectivity

analyses revealed differences in connectivity between the groups, particularly within and between the basal ganglia, insula, and prefrontal cortex.
Conclusions: Children with ADHD and comorbid aggression have reduced gray matter volume within emotional processing regions and the basal ganglia. Preliminary findings suggest similar abnormalities in functional connectivity. Etiological and treatment implications will be discussed

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J Am Acad Child Adolesc Psychiatry. 2017;56:S164.

PHYSICIAN PEER-INFLUENCE ON PRESCRIBING PSYCHOTROPIC POLYPHARMACY IN THE TREATMENT OF CHILDREN AND ADOLESCENTS WITH MENTAL DISORDERS.

Upadhyay N, Medhekar RA, Fujimoto K, et al.

Objectives: The goal of this session is to examine the effect of physician's peer influence on the prescription of psychotropic polypharmacy (PP) among children and adolescents treated for mental disorders (MD).
Methods: A retrospective study was conducted using the 2013-2015 administrative claims data from Texas Children's Health Plan. The study included the following individuals: 1) aged-18 years; 2) diagnosed with MD; and 3) received psychotropic prescriptions from a single prescriber during the study period. The outcome of interest was PP, defined as the receipt of two or more psychotropic medications from different drug classes concurrently for-60 days. Multilevel generalized linear-mixed model was used to study the association between physician-level, peer-influence measures, and patient-level risks of receiving PP by adjusting for the practice-, physician-, and patient-level covariates. This study measured physician peer influence using social network measures. Two network measures were used: affiliation exposure (AE) and structural equivalence (SE). AE represents the extent to which a physician is exposed to the PP-prescribing behavior of other physicians via sharing of patients. SE measures the degree to which a physician is exposed to the PPprescribing behaviors of their structurally equivalent peers.
Results: Children and adolescents (N = 24,147) had a diagnosis of MD and received at least one psychotropic medication. Of this population, 13,045 (54.02%) met the study inclusion criteria. The multilevel models found that as a physician is exposed more to their peers prescribing PP through the sharing of same patients (AE), there is 77 percent higher likelihood for their patients to receive PP (OR = 1.766; 95% CI 1.027-3.037); in addition, as physicians occupy more comparable position in patient-sharing network to other physicians prescribing PP (SE), the higher the likelihood of their patients receiving PP (OR = 4.236; 95% CI 2.071-8.666). Physician specialty and patient-level factors, including gender, race, and diagnosis of ADHD, bipolar disorder, and depression, were associated with prescription of PP.
Conclusions: Physician peer influence was strongly associated with PP, implying that targeting and changing the prescribing behaviors of guideline non concordant physicians could be useful in enhancing the diffusion of guideline-concordant practices among other physicians

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J Am Acad Child Adolesc Psychiatry. 2017;56:S288.

NATIONAL PATTERNS OF MALADAPTIVE BEHAVIORS IN ADOLESCENTS WITH ADHD.

Sultan R, Olfson M.

Objectives: The purpose of this study is to assess and compare the risk of maladaptive behaviors in adolescents with and without ADHD.
Methods: Data were analyzed from the National Comorbidity Survey Adolescent Supplement (NCS-A), a nationally representative survey of 10,123 adolescents with DSM-IV mental, emotional, and behavioral disorders and service use. The total percentages and odds ratios were compared over lifetime for adolescents with and without ADHD in multiple domains including: 1) suicide; 2) aggression; 3) behavior regulation; 4) recent life events; 5) education; and 6) substance use.
Results: ADHD is associated with an elevated risk for a range of maladaptive behaviors. For instance, adolescents with ADHD had suicide attempts at a rate of 7.4 percent versus 3.4 percent of control subjects [adjusted OR (aOR) 2.9, 95% CI=1.3-6.6]. Fifty-seven percent of youth with ADHD had a history of physical aggression toward others as compared with 37.5 percent of controls (aOR 2.1, 95% CI=1.6-2.6). Adolescents

with ADHD were more likely to have been expelled from school or fired from a job (8.9% vs 2.4%), (aOR 3.3, 95% CI=1.7-6.5). Adolescents with ADHD (11.6%) compared with controls (6.0%) reported more lifetime history of problems from drinking (aOR 1.9, 95% CI=1.2-2.9).
Conclusions: Adolescents with ADHD are at elevated risk for many maladaptive behaviors that have the potential to significantly alter the long term trajectory of their lives

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J Am Acad Child Adolesc Psychiatry. 2017;56:S327.
DEVELOPMENTAL PERSPECTIVES ON AGGRESSION AND DISRUPTIVE BEHAVIORS AND IMPLICATIONS FOR TREATMENT.
Newcorn J, Ivanov I.
Objectives: Aggression is a behavioral trait that is present from early development and may follow various developmental trajectories. Aggressive behaviors are robustly present in youth diagnosed with disruptive behavior disorders (DBD), such as ADHD, ODD, and conduct disorder (CD); moreover, the link between childhood DBDs and later antisocial personality disorder (ASPD) has been well documented. However, the underlying neurobiological mechanisms that may either facilitate or offer protective effects on the transition from childhood DBD to ASPD are poorly understood. This symposium will discuss new findings from naturalistic and experimental studies that have examined the neurobiological substrates of aggressive behaviors and related diagnoses and consider implications for treatment of this population.
Methods: Participants in these studies include both children and adolescents who have been followed longitudinally or have participated in various clinical or neuroimaging protocols. Participants in the neuroimaging studies had comprehensive assessments followed by pharmacological challenge or ongoing treatment; fMRI scans were performed using different reward processing and inhibitory control tasks.
Results: Findings indicate that low serotonergic reactivity in children with ADHD may predict later ASPD, and a variety of neuroregulatory deficits are present in youth with aggression and DBDs. This includes both volumetric abnormalities and aberrant functional connectivity linking prefrontal cortex, limbic structures, and striatum. Stimulant and nonstimulant medications can potentially have a role in treating aggression and DBDs in youth with ADHD, and the best predictive model highlights the inter-relationships among ADHD symptoms, aggression, and mood dysregulation.
Conclusions: This symposium will present the results of several studies indicating the neurobiological basis of aggression and disruptive behavior disorders in youth with ADHD. Etiological factors relevant to the developmental trajectories of aggression, relations to adult psychopathology, and possible treatments for aggression will be discussed

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J Am Acad Child Adolesc Psychiatry. 2017;56:S148.
DIAGNOSING CO-OCCURRING MENTAL DISORDERS IN CHILDREN AND ADOLESCENTS WITH INTELLECTUAL DISABILITY/INTELLECTUAL DEVELOPMENTAL DISORDER.
Munir KM.
Objectives: This presentation describes the co-occurrence and assessment of mental disorders (MD) in children and adolescents with intellectual disability (ID) and intellectual developmental disorders (IDD). The presentation offers modifications in assessment techniques for differential diagnosis of MD, with a particular emphasis on DSM-5 conceptualization of ID and IDD that include both intellectual and adaptive functioning deficits.
Methods: The clinical and epidemiological literature on MD in children and adolescents with ID/IDD is reviewed. The modifications for assessment of MD in ID/IDD include the following: the use of broad-and narrow-band behavior rating scales of symptoms and symptom domains, any corresponding DSM scales, and use of multiple informant sources; direct and indirect interview techniques, with special attention to modifications for use with nonverbal children and adolescents; and consideration of neurological, medical, and genetic syndromes that may transform expression of co-occurring MD.
Results: Children and adolescents with ID/IDD are at greater risk for MD compared with the general population. Both the prevalence and clinical presentation of MD are modified by child and adolescent age,

gender, and ID/IDD severity. Most common MD in children and adolescent with ID/IDD include the following: other neurodevelopmental disorders (e.g., ASD, ADHD, specific learning, and stereotyped movement with and without self-injurious behaviors, and other specified and unspecified neurodevelopmental disorders); anxiety, depression, mood disorder, psychosis, and trauma-and stressrelated disorders; OCD-related disorders; and disruptive, impulse-control, and conduct disorders. Pitfalls in diagnosis include an over-reliance on the use of partial criteria, incomplete review of the overarching clinical syndrome, short-circuiting of differential diagnosis, and premature use of psychopharmacological interventions that may alter manifestation of MD and delay their targeted treatment.
Conclusions: The diagnosis of MD in children and adolescents with ID/IDD entail a systematic review of multiple factors within a requisite biopsychosocial framework and integrated consideration of home, education, and social environments

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J Am Acad Child Adolesc Psychiatry. 2017;56:S234.

FACE EMOTION RECOGNITION DIFFERENCES WITH RESPECT TO FRUSTRATION IN DISRUPTIVE MOOD DYSREGULATION DISORDER (DMDD) AND ATTENTION-DEFICIT/HYPERACTIVITY DISORDER (ADHD).

Taskiran S, Turkakin E, Karamanci C, et al.

Objectives: We examined the effect of frustration in emotion recognition across children with ADHD and disruptive mood dysregulation disorder (DMDD) and healthy control (HC) subjects.
Methods: Sample group consisted of 43 participants (14 DMDD + ADHD, 14 ADHD, 15 HC subjects, mean = 9.51; SD = 2.10), who completed a novel emotion recognition task with a frustration component that we developed using happy, angry, and neutral faces from the FACES database of Max Planck Institute for Human Development. The task was a two-alternative forced choice paradigm in which participants were asked to identify if a face was happy versus neutral or if a face was angry versus neutral. Frustration, in some blocks, was elicited by providing conflicting feedback and holding back deserved points after some correct answers.
Results: In the frustration blocks of the emotion recognition task, there were statistically significant main effects of emotion on accuracy [$F(1,39) = 18.886$, $P < 0.001$, $h2 = 0.326$] and the type of feedback in previous trial on the response time [$F(1,39) = 11.019$, $P < 0.002$, $h2 = 0.220$], as well as a between-subjects effect of diagnosis on accuracy [$F(2,39) = 6.384$, $P = 0.004$, $h2 = 0.247$]. Post hoc analyses revealed that participants were more accurate recognizing happy faces as opposed to angry faces ($P < 0.001$), slower after frustrating trials ($P = 0.002$), and that participants with DMDD were less accurate than control subjects ($P = 0.017$) and participants with ADHD ($P = 0.007$). Linear integrated speed-accuracy scores (LISAS), interpreted as reaction time adjusted by error rate, showed a main effect of emotion [$F(1,39) = 12.389$, $P = 0.001$, $h2 = 0.241$] and feedback type in previous trial [$F(1,39) = 6.350$, $P = 0.016$, $h2 = 0.140$], but there was no between-subjects effect of diagnosis group on LISAS. The post hoc analyses revealed that the reaction time adjusted for error rates when recognizing happy faces were found to be faster as opposed to angry faces ($P = 0.001$) and slower in postfrustration trials ($P = 0.016$).
Conclusions: Children with DMDD are less accurate overall compared with healthy control subjects and children with ADHD in the novel task that involves emotion recognition. Their impairment becomes more pronounced after frustrating trials, which emerge as a distinctive feature between participants with pure ADHD and those with ADHD/DMDD comorbidity

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J Am Acad Child Adolesc Psychiatry. 2017;56:S289.

PHARMACOGENOMICS OF METHYLPHENIDATE SIDE EFFECTS IN CHILDREN WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER (ADHD).

Wagner-Schuman ML, Froehlich TE, Kottyan LC, et al.

Objectives: Because of significant individual variability in the side effects of ADHD medication, there is increasing interest in identifying genetic predictors of adverse effects. This study uses a novel high-

throughput genomic sequencing tool (PGRNseq) to identify predictors of side effects of methylphenidate (MPH) in children with ADHD.
Methods: Stimulant-na+»ve children (ages 7-11 years; n = 108, mean age = 8.5 years, 74% male) participated in a randomized, double-blind, placebocontrolled trial of long-acting MPH. Caregivers completed weekly ratings of irritability, sleep, and appetite using Pittsburgh Side Effect Rating Scale items. We sequenced DNA from saliva samples from 108 participants of European ancestry using the PGRNseq platform, which analyzes 82 genes previously identified as potentially important pharmacogenes. We selected 2,814 of 3,356 useful markers after exclusion of markers with missing rates of >5 percent, Hardy-Weinberg Equilibrium P < 5 10 4, or minor allele frequency <2 percent. We performed association tests of the side effects of irritability, sleep problems, and decreased appetite for each participant on the highest MPH dose administered (36 mg for children <25 kg and 54 mg for children >25 kg) on the 2,814 markers using a linear regression additive model, adjusting for MPH dose and baseline (premedication) rating.
Results: Although no associations met the Bonferroni-corrected P < 1.8 10 5, our strongest findings included an association between a taurine transporter SLC6A6 variant (rs2341970) and the MPH side effect of irritability (P = 7 10 5) and an association between a carboxylesterase 1 (CES1) variant (rs200464425) and MPH-related sleep problems (P = 1 10 4).
Conclusions: This hypothesis-generating study identified two genetic variants that may help predict individuals who are more likely to experience irritability and sleep problems with MPH treatment. Given evidence of SLC6A6 as a gaminobutyric acid (GABA) transporter and effects of the GABA system on irritability, the role of SLC6A6 in this MPH side effect is plausible. Effects of CES1 variants on sleep are also plausible given CES1's role in MPH metabolism

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J Am Acad Child Adolesc Psychiatry. 2017;56:S95.

MOODINESS RELATED TO ANXIETY AND OBSESSIVE-COMPULSIVE DISORDERS IN CHILDREN WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.

Spaniardi A.

Objectives: ADHD and anxiety disorders are the most common mental health disorders found in children and can often co-occur. OCD is also frequently comorbid with ADHD. Both anxiety disorders and OCD can present with ADHD-like symptoms, which makes a correct diagnosis more challenging. Participants in this talk will learn rational approaches to distinguishing these complex symptoms in the evaluation of children with ADHD and comorbid anxiety or OCD. Participants will also be able to describe our current knowledge about the implementation of therapy and pharmacology in patients with ADHD and these comorbidities.
Methods: This presentation will review and discuss the literature on biology, diagnosis, and treatment of children with ADHD and comorbid OCD or anxiety disorders. The neurobiology, correlates, and risk factors of these disorders will be discussed. Information from this presentation will be drawn from a literature review of randomized controlled trials, case studies, and meta-analyses.
Results: Evidence shows that the presence of anxiety or OCD comorbid with ADHD can alter the etiology, correlates, and response to medications and therapy. There is increasingly strong evidence for the role of pharmacotherapy, psychosocial treatments, and the combination of these forms of treatment in comorbid patients with ADHD. Through this presentation, participants will gain in knowledge and improve their management of these comorbidities with ADHD.
Conclusions: Participants will be better able to use strategies for the evaluation of children with ADHD with comorbid anxiety disorders and OCD. Participants will also learn evidence-based strategies for treating such patients with ADHD and these comorbidities in their clinical practice

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J Am Acad Child Adolesc Psychiatry. 2017;56:S289-S290.

A CASE SERIES OF OMEGA-3 FATTY ACIDS SUPPLEMENTATION IN MEDICATED CHILDREN WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER AND DEFICITS IN EMOTIONAL SELFREGULATION.

Wilens TE, Carrellas NW, Zulauf C, et al.

Objectives: Recent work has demonstrated that treated and untreated individuals with ADHD have elevated rates of deficits in emotional self-regulation (DESR). However, few treatment options specifically targeting DESR in ADHD exist. Omega 3 fatty acids (FA) have been shown to reduce mood dysregulation. We aimed to evaluate the effectiveness of adjunct omega-3 fatty acids treatment in children with co-occurring ADHD and DESR.

Methods: Children aged six to 17 years who carried an established diagnosis of ADHD and were receiving medication for their ADHD prior to screening were enrolled. Omega-3 FA (975 mg eicosapentaenoic acid) was administered openly up to 12 weeks supplemental to subjects' ADHD medication. Primary outcomes included Clinical Global Impression (CGI) scales for ADHD and DESR, and the Behavior Rating Inventory of Executive Functioning (BRIEF). All analyses were intention to treat with the last observation carried forward for subjects that did not complete the full study schedule. A series of paired sample t-tests were conducted to compare the pre- and post-treatment scores of the outcome measures. All tests were 2-tailed, and significance was determined at a=0.05.

Results: Twenty-one subjects signed consent and were enrolled. Of those that enrolled, several did not participate after signing consent (n = 7), were lost to follow-up after the baseline visit (n = 1), or discontinued by the investigator due to protocol requirements (n = 2). Our final sample (n = 10) included 7 subjects who completed the study, and 3 subjects who finished study measures through week six of the 12-week trial (60% male; mean age 10.6 2.6 years). By CGI-Improvement, 70 percent of subjects were DESR responders with reduced CGI-DESR Severity scores (4.6 0.7 to 3.0 0.9; p<0.0001). While we found improvement trends on the major indices of the BRIEF; there was no significant improvement in ADHD. Overall, the omega-3 fatty acids were well tolerated.

Conclusions: Our findings from a small case series of omega-3 fatty acids supplementation to ADHD medication in children with ADHD and DESR showed improvements in mood (DESR) but not ADHD. These pilot data provide encouraging support for a larger controlled trial of omega-3 fatty acids as adjunct therapy for residual DESR in treated ADHD youth

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J Am Acad Child Adolesc Psychiatry. 2017;56:S273.

EFFECTS OF CHILDHOOD ADHD ON DRIVING OUTCOMES: LESSONS FROM THE MULTIMODAL TREATMENT OF ADHD STUDY (MTA).

Roy A, Epstein J, Garner A, et al.

Objectives: The goal of this session is to assess a range of driving outcomes in the Multimodal Treatment Study of ADHD (MTA) sample group. We hypothesize higher levels of accidents and driving infractions in the following: 1) individuals with ADHD compared with no ADHD; and 2) persistent ADHD compared with desistent ADHD.

Methods: Participants with (n = 579) and without (n = 258) childhood ADHD from the MTA (a 14-month randomized treatment study with observational follow-ups for 16 years, covering ages 9-25 years and with driving assessments from age 15 years onward) were assessed for car crashes and police involvement in driving infractions between licensure and age 25 years. Group differences in number of crashes and police involvement were assessed, accounting for driving experience.

Results: Participants with childhood ADHD report higher numbers of accidents and police involvement in infractions of speeding, driving without a seat belt, using a cell phone while driving, and not yielding right-of-way than matched control subjects. No differences were found for persistent vs. desistent ADHD. Participants with childhood ADHD also have higher car crashes per month of driving experience. Only individuals with persistent ADHD, but not desistent ADHD, had a higher rate of car crashes than control subjects.

Conclusions: Childhood ADHD is associated with a high risk for poor driving behaviors, when accounting for driving experience, and is independent of ADHD symptom persistence. However, involvement in car accidents is associated with persistence of ADHD into adulthood

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J Am Acad Child Adolesc Psychiatry. 2017;56:S212.

AT-HOME FUNCTIONAL IMPAIRMENT IN YOUTH WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER (ADHD): FACTOR STRUCTURE AND NORM-REFERENCED CUT-OFF POINTS FOR THE BEFORE SCHOOL FUNCTIONING QUESTIONNAIRE AND PARENT RATING OF EVENING AND MORNING BEHAVIOR SCALE, REVISED.

Faraone SV, DeSousa NJ, Nullmeier R, et al.

Objectives: Two validated rating scales provide measures of temporal athome functional impairment for clinical trials in children with ADHD: 1) Before School Functioning Questionnaire (BSFQ), which assesses early morning functional (EMF) impairment; and 2) Parent Rating of Evening and Morning Behavior Scale, Revised (PREMB-R), which evaluates EMF and late afternoon/evening functional impairment. The objectives of this study were to determine the factor structure and define norm-referenced cut-off points for both instruments.

Methods: A survey was conducted with 1,200 respondents derived from a representative US sample of primary caregivers of youth (aged 6-17 years; n = 50 per age/gender category). Caregivers were enrolled if their child never had ADHD or had a history of ADHD (past or current untreated). Using a severity scale of 0 to 3 (higher score indicating greater severity), caregivers rated their child's at-home functional impairment on the 20-item BSFQ and 11-item PREMB-R. Factor analyses were conducted, and percentile cut-off points were calculated for screening risk (80th) and for identifying mild (90th), moderate (93rd), and severe (97th) functional impairment.

Results: Of the 700 children (aged 6-12 years) and 500 adolescents (aged 13-17 years) rated by a caregiver, 1,079 had no history of ADHD and 121 had a history of ADHD. As expected, BSFQ fit a 1-factor model, which explained 91.7 percent of the variance, and PREMB-R fit a 2-factor model, with one factor containing three morning items (PREMB-R AM subscale) and the other accounting for eight late afternoon/evening items (PREMB-R PM subscale). Age and comorbidities, but not gender, had significant effects on scores. Youth with ADHD had significantly higher scores than those without ADHD, even after adjusting for comorbidities. Norm-referenced cut-off points were defined for screening risk (BSFQ: 24; PREMB-R AM: 4; PREMB-R PM: 10), and for mild (BSFQ: 32; PREMB-R AM: 6; PREMB-R PM: 14), moderate (BSFQ: 36; PREMB-R AM: 6; PREMB-R PM: 16), and severe (BSFQ: 41; PREMB-R AM: 7; PREMB-R PM: 18) functional impairment. Cut-offs are also presented by age.

Conclusions: Percentile cut-off points derived from norm-referenced data are defined to guide clinicians in determining the severity of ADHD-related athome functional impairment among youth

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J Am Acad Child Adolesc Psychiatry. 2017;56:S212-S213.

PSYCHOMETRIC VALIDATION OF THE BEFORE SCHOOL FUNCTIONING QUESTIONNAIRE AND PARENT RATING OF EVENING AND MORNING BEHAVIOR SCALE, REVISED IN CHILDREN WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER (ADHD).

Faraone SV, DeSousa NJ, Sallee FR, et al.

Objectives: The goals of this session are to assess the psychometric properties of the Before School Functioning Questionnaire (BSFQ) and Parent Rating of Evening and Morning Behavior Scale, Revised (PREMB-R) and determine the following: 1) whether the previously validated BSFQ and PREMB-R morning (ante meridiem, AM) subscales are measuring the same construct [early morning functional (EMF) impairment]; and 2) whether the PREMB-R evening (post meridiem, PM) subscale is a valid and reliable measure of late afternoon/evening functional impairment in children with ADHD.

Methods: Using data from two randomized, placebo-controlled phase 3 trials of HLD200 in children (ages 6-12 years) with ADHD, reliability (internal consistency and test-retest) and construct validity (convergent/divergent and known groups) were evaluated by correlating or comparing BSFQ, PREMB-R AM,

and PREMB-R PM scores with other instruments [ADHD Rating Scale-IV (ADHD-RS-IV); ADHD-RS-IV between 6:00 AM and 9:00 AM (ADHD-AM-RS); Clinical Global Impression-Improvement (CGI-I) and Clinical Global Impression-Severity (CGI-S); Connors' Global Index-Parent (CGI-P); Swanson, Kotkin, Agler, M-Flynn, and Pelham (SKAMP); and Permanent Product Measurement of Performance (PERMP)].
Results: BSFQ and PREMB-R AM/PM scales demonstrated strong internal consistency (Cronbach's a >0.7) and at least good test-retest reliability (intraclass correlation coefficient >0.7, except 0.59 for PREMB-R AM scale in one trial). BSFQ and PREMB-R AM had moderate to large correlations with ADHD-AM-RS and with one another, small to moderate correlations with ADHD-RS-IV, and no correlations with SKAMP and PERMP. PREMB-R PM scales had moderate correlations with ADHD-RS-IV, ADHD-AM-RS, and BSFQ and no correlations with SKAMP or PERMP. With increasing ADHD severity (measured by CGI-S, CGI-P, and ADHD-RS-IV), mean BSFQ ($P < 0.0005$), PREMB-R AM ($P < 0.03$), and PREMB-R PM ($P < 0.0001$) scores were higher (worse) with significant linear trends across the groups. Significant positive correlations between mean change scores from baselines in BSFQ, PREMB-R AM, and PREMB-R PM and other measures (ADHD-RS-IV, ADHD-AM-RS, CGIP, CGI-I) were found in both trials (all $P < 0.0001$).
Conclusions: These findings psychometrically support the use of BSFQ and PREMB-R AM/PM scales in clinical trials of children with ADHD and demonstrate that BSFQ and PREMB-R AM scales measure the same underlying construct (EMF impairment)

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J Am Acad Child Adolesc Psychiatry. 2017;56:S77.

PEDIATRIC BIPOLAR DISORDERS AND ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.

Diler RS.

Objectives: Studies identified significant comorbidity of ADHD in youth with bipolar disorder (BD). Early recognition and treatment of mania is of vital importance to ameliorate ongoing syndromal and subsyndromal symptomatology and to reduce psychosocial morbidity and risk for suicide. We aim to characterize a clinical picture of manic presentations and longitudinal course in youth with ADHD that can help improve correct diagnoses and treatment interventions.
Methods: Clinical characteristics of mania and depression in youth with BD and without ADHD and longitudinal trajectories of ADHD and BD will be reviewed. Baseline and repeated assessments at inpatient and outpatient settings will be reviewed, focusing on symptoms that help improve discriminating BD.
Results: Recent studies have shown that BD is mainly manifested by recovery and recurrences, but ongoing fluctuating mood symptomatology, especially subsyndromal depressive and mixed symptoms, is also very common. Clinicians must be cautious about attributing symptoms to mania or hypomania unless they show a clear temporal association with the abnormally elevated, expansive, and/or irritable mood (plus increased activity/energy levels). The requirement of change in energy/activity levels in the DSM-5 for diagnosis of mania has important clinical implications in youth with ADHD. Symptoms of irritability, inattentiveness, and hyperactivity should be carefully assessed, with longitudinal follow-up to ascertain whether these symptoms are indeed manifestations of BD (e.g., clustering of other manic symptoms, change from baseline, and functional impairment). Presence of ADHD in youth with bipolar spectrum disorders is associated with worse mood swings during follow-up. Treatment of ADHD may benefit from stimulants after stabilizing the mood first.
Conclusions: Careful clinical assessment can help improve identification of BD in youth with ADHD, which has significant treatment implications. We know very little about mixed mood presentations and medication effect on longitudinal outcomes, and future studies evaluating possible preventative strategies for youth with ADHD and at high risk for BD are indicated

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J Am Acad Child Adolesc Psychiatry. 2017;56:S283.

FACTORS THAT AFFECT THE ADHERENCE TO ATTENTION-DEFICIT/HYPERACTIVITY DISORDER (ADHD) MEDICATIONS DURING A TREATMENT CONTINUATION PERIOD IN CHILDREN AND ADOLESCENTS: A NATIONWIDE RETROSPECTIVE COHORT STUDY USING KOREAN HEALTH INSURANCE DATA FROM 2007 TO 2011.

Hwang J-W, Bhang S-Y.

Objectives: Several factors, such as male gender, older age, type of insurance, comorbid conditions, and medication type, have been associated with ADHD medication adherence rates, but the results have been inconsistent. This study aimed to explore what factors were associated with ADHD medication adherence.

Methods: We analyzed Korean National Health Insurance data, which comprised continuously enrolled Korean National Medical Insurance children (aged 6-18 years) with at least two ADHD prescription claims (January 2008-December 2011). The persistence of use regarding the days of continuous therapy without a 30-day gap were measured continuously and dichotomously. Adherence, using a medication possession ratio (MPR), was measured dichotomously (80% cut-off).

Results: In the multivariate logistic analysis of persistence (30-day gap), having national medical insurance lowered the odds by 0.784 compared with Medicaid, and treatment in an urban area or private clinic increased the odds by 1.07 or 0.651, respectively. In addition, psychiatric comorbidity increased the odds by 1.204 compared with no psychiatric comorbidity. Regarding analysis of the MPR (80% cut-off), odds were increased by treatment by a specialist (1.4), treatment at a private clinic (1.47), and psychiatric comorbidity (1.301).

Conclusions: A better understanding of ADHD treatment patterns may lead to initiatives targeted at the improvement of treatment adherence and persistence. Other factors, including the severity, family history, costs, type of comorbidities, and switching patterns, will be analyzed in future studies. PPC, ADHD, STIM

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J Am Acad Child Adolesc Psychiatry. 2017;56:S284.

PREDICTORS OF LONG-TERM RISKY DRIVING BEHAVIOR IN THE MULTIMODAL TREATMENT STUDY OF CHILDREN WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER (ADHD).

Johnson JA, Jakubovski E, Reed MO, et al.

Objectives: The purpose of this study was to examine predictors of later risky driving behavior in children with ADHD.

Methods: Stepwise logistic regression and receiver operating characteristic (ROC) analyses were used to explore baseline predictors of risky driving behavior for adolescents that completed the eight-year follow-up assessment in the Multimodal Treatment Study of Children with Attention-Deficit/Hyperactivity Disorder (MTA).

Results: Stepwise logistic regression analysis explained 19 percent of the total variance in risky driving behavior. Increased likelihood of risky driving behavior was associated with parental history of conduct disorder, low parental monitoring and supervision, and increased age. ROC analysis identified discriminative predictors for adolescents older and younger than age 16 years at follow-up. The most discriminative predictors of later risky driving behavior were parental stress at baseline (children 16 years) and increased child-rated parental protectiveness (children < 16 years).

Conclusions: Risky driving behavior was significantly predicted by baseline characteristics for the MTA cohort. Aspects of parenting behavior (or the child's perception of them) including parental stress levels, parental protectiveness, and parental levels of monitoring and supervision were most informative in predicting these outcomes. Our results suggest interventions to reduce high-risk behaviors in these high-risk children with ADHD might involve targeted parenting interventions

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J Am Acad Child Adolesc Psychiatry. 2017;56:S283-S284.

A DOUBLE-BLIND, PLACEBO-CONTROLLED, DOSE-RANGING STUDY OF EXTENDED-RELEASE VILOXAZINE (SPN-812 ER) IN CHILDREN WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER (ADHD).

Johnson JK, Saylor K, Brittain ST, et al.

Objectives: The purpose of this study was to determine the effective and safe doses of once-daily, extended-release viloxazine (SPN-812 ER), a structurally distinct, bicyclic norepinephrine reuptake inhibitor, in children aged 6-12 years with ADHD.

Methods: In a randomized, double-blind, placebo-controlled, multicenter, 5-arm, parallel-group, dose-ranging study, 217 randomized subjects received either placebo or active treatment (SPN-812 ER 100, 200, 300, or 400 mg) at 1:2:2:2:2. Treatment continued for a total of eight weeks (including three weeks of titration). The primary endpoint was change from baseline (CFB) to end of study in the ADHD Rating Scale-IV (ADHD RS-IV) Total Score. Clinical Global Impression -Severity (CGI-S) and -Improvement (CGI-I) scores were secondary measures. Safety assessments included laboratory and ECG measurements, and reporting of adverse events (AEs).

Results: Mean CFB in ADHD RS-IV Total Scores for the intent-to-treat population (n = 206) improved in all SPN-812 ER dose groups compared to placebo, and differences were statistically significant in the 200 (p = 0.031), 300 (p = 0.027), and 400 mg dose (p = 0.021) groups [CFB Least Squares Means (LsMeans)=(-18.4), (-18.6), and (-19.0); LsMean for placebo=(-10.5)]. Similar results were observed for the CGI-S whereas CGI-I improvement was significant only for the 300-mg group. The most frequent treatment-emergent AEs (15.0% of subjects) were somnolence, headache, and decreased appetite, with the incidence increasing with higher SPN-812 ER doses.

Conclusions: Treatment with 200, 300, and 400 mg SPN-812 ER resulted in statistically significant improvement in CFB in ADHD RS-IV Total Scores compared to placebo; the primary efficacy results were confirmed by sensitivity analyses and are supported by results from analyses of secondary efficacy measures. All SPN-812 ER doses tested were well tolerated. SPN-812 ER will be further evaluated as a non-stimulant pharmacotherapy for the treatment of ADHD

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J Am Acad Child Adolesc Psychiatry. 2017;56:S282-S283.

COMPARISON OF SUICIDAL IDEATION, BULLYING, AND BULLIED EXPERIENCE BETWEEN GENERAL STUDENTS AND ATTENTION-DEFICIT/HYPERACTIVITY DISORDER (ADHD) PATIENTS.

Huh SY, Kim J-H, Choi B-S, et al.

Objectives: Impulsivity is one of the core symptoms in ADHD and makes it easier to become a victim or assailant of bullying. Impulsivity and bullied experiences are among the most important risk factors for suicide of school age youth. The purpose of this study is to compare suicide ideation, bullying, and bullied experiences between normal school-age youths and patients with ADHD.

Methods: The subjects of this study were classified into patient group and control group. Patient group were 62 outpatients or inpatients to the Department of Pediatric Psychiatry, Pusan National University Yangsan Hospital, and 49 patients diagnosed with ADHD were selected. The control group comprised 3,727 youths in elementary, middle, and high schools of the metropolitan city of Busan who were asked to fill out questionnaires. Of the 1,717 respondents, 245 were selected for patient-controlled studies. All the subjects were asked to complete the Beck Suicide Ideation Scale, the State-Trait Anxiety Inventory, and report on bullying and bullied experiences. Bullied experiences were measured using Likert scale of get heavy teasing or mocking, getting bullied, beating from others, and deprived from others. Bullying experiences were measured using Likert scale of doing heavy teasing or mocking, bullying, beating others, and depriving from others. The rates of suicide ideation, and bullying and bullied experiences between ADHD group and the control group were compared using the Chisquare test (c2 test). All analyses were conducted using SPSS software version 24, and $P < 0.05$ was considered statistically significant.

Results: There were significant differences between the ADHD group and normal control group in suicide ideation, getting bullied experiences ($p < 0.05$) but not significant for bullying experiences ($p > 0.05$).

Conclusions: The symptoms of ADHD might play a significant role in the development of suicide ideation and bullied experiences in school-age youth with ADHD. Appropriate management of ADHD symptoms are needed to reduce suicidal ideation and getting bullied experience in school-age youth with ADHD

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J Am Acad Child Adolesc Psychiatry. 2017;56:S279-S280.

DISRUPTIONS IN GLUTAMATERGIC NETWORK AND NEURONAL CONNECTIVITY GENES IN CHILDREN AND ADOLESCENTS WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER (ADHD): POSSIBLE ASSOCIATION WITH EMOTIONAL DYSREGULATION.

Elia J, Kim C, Khan M, et al.

Objectives: The goals of this presentation are as follows: 1) to estimate prevalence of rare, recurring copy number variants (CNVs) of glutamatergic network genes (e.g., metabotropic glutamate receptor genes, GRMs), and neuronal connectivity genes (e.g., contactin 4, CNTN4); and 2) to characterize associated behavioral phenotypes in a pediatric population with ADHD, comparing CNV-positive (CNV+) versus CNV-negative (CNV) subjects.

Methods: Multicenter (n = 32), noninterventional study enrolled children and adolescents with ADHD, collecting saliva samples for analysis (273 genes) by Children's Hospital of Philadelphia genotyping laboratory. A questionnairedirected interview assessed phenotype: ADHD symptoms, medical history, ADHD treatment history, mental illness comorbidity, development/education history, and current behaviors of concern. Post hoc analyses of specific gene subsets were conducted (e.g., CNTN4, which encodes cell adhesion molecule involved in neuronal network formation and plasticity). CNTN4 disruptions are associated with neurodevelopmental disorders (e.g., autism spectrum disorder).

Results: Of 1,876 subjects, the CNV+ prevalence was 22 percent (n= 420). Most notable differences between CNV cohorts were as follows: higher proportion of black/African American subjects in CNV+ cohort (35 vs. 18%); CNV+ status associated with significantly higher occurrence of parent-reported emotional dysregulation (disruptive behavior $P < 0.001$; anger control, $P < 0.05$); and inappropriate movements ($P < 0.01$). CNVs most commonly involved CNTN4, comprising 22 percent (n=92) of CNV+ cohort; and 73 percent of CNTN4 CNV+ was black/African American. Parent concerns were cited significantly more often forCNTN4 CNV+ cohort: disruptive behavior ($P<0.001$); completing work ($P = 0.007$); anger control ($P = 0.004$); risk taking ($P = 0.005$); inappropriate movements ($P = 0.015$) and sounds ($P = 0.03$); and hyperactivity ($P = 0.04$).

Conclusions: Mutations in glutamatergic network and neuronal connectivity genes of interest, particularly CNTN4, in children and adolescents with ADHD were associated with an increased risk of parent-reported emotional dysregulation. The CNTN4 CNV+ phenotype suggests a more vulnerable population at risk for poor ADHD outcomes. Further investigation of this population is planned

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J Am Acad Child Adolesc Psychiatry. 2017;56:S144-S145.

WHAT'S NEW IN SUBSTANCE USE DISORDERS, CIGARETTE USE, AND ATTENTION-DEFICIT/HYPERACTIVITY DISORDER IN ADOLESCENTS?

Wilens TE.

Objectives: The goal of this session is to review articles chosen by the Work Group on Lifelong Learning addressing current concepts and understanding in the following areas: 1) longer-term course of ADHD; 2) a trial of combination pharmacotherapy in ADHD; 3) tobacco use in adolescents; 4) opioid use in young people; and 5) effects of cannabis in adolescents.

Methods: This presentation reviews articles from the following perspectives: importance/context; participants; hypotheses, study design, and findings; implications for clinical practice; limitations; and recommendations for future practice and research.

Results: The studies report the following: 1) approximately 50 percent of children with ADHD will persist with the disorder into adulthood with noted predictors of remission-those with remitted ADHD fared better than those with persistent ADHD; 2) the combination of guanfacine plus methylphenidate is more efficacious than either treatment alone; 3) tobacco use is common in adolescents-particularly those with comorbid

psychopathology; 4) opioid use often initiates in childhood and is associated with high rates of morbidity and mortality in young people; and 5) cannabis use in adolescents is associated with neurocognitive difficulties that may persist into later adulthood. The risk of psychotic symptoms seems to be directly related to cannabis use in young people.
Conclusions: Many children with ADHD continue to have persistent ADHD into adulthood with persistence associated with generally more problematic outcomes. When combined with stimulants, guanfacine is more effective than monotherapy with either treatment alone. Tobacco disorders are common in youth, particularly those with dual diagnosis. Opioid use disorders in youth are increasing, with severe morbidity and mortality associated with them. Recreational cannabis use in adolescents is linked to a number of problematic outcomes, including higher rates of psychotic symptoms. Effective treatments exist for cannabis use disorders

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J Am Acad Child Adolesc Psychiatry. 2017;56:S278.

ATTENTION-DEFICIT/HYPERACTIVITY DISORDER (ADHD): A SURVEY OF KNOWLEDGE AND ATTITUDES AMONG PEDIATRIC RESIDENTS IN LAHORE, PAKISTAN.

Raza F, Azeem MW, Imran N, et al.

Objectives: ADHD is a prevalent global condition. In Pakistan, pediatricians are often the first to encounter affected children. Unfortunately, they receive little education in child and adolescent psychiatry during their training; thus, many children remain undiagnosed and untreated. Therefore, this study aimed to assess the knowledge and attitudes of pediatric residents toward ADHD and its management.
Methods: Following institutional review board approval, a self-administered questionnaire on ADHD was distributed among pediatric residents enrolled in all four years of training in all seven public sector-teaching hospitals of Lahore, Pakistan. The survey collected demographic information and tested their knowledge and views on the psychological, diagnostic, treatment, and prognostic aspects of the disorder.
Results: Surveys were completed by 205 pediatric residents (N = 245; response rate = 83.6%). The mean age of the respondents was 27.5 years (SD = 2.2), and 57.1 percent were males. Only 16.0 percent stated that they had adequate knowledge about the disorder. Misconceptions regarding some of the etiologic features of ADHD were observed. Some respondents (62.0%) believed that poor parenting and parental spoiling could cause ADHD, and 62.7 percent stated that children with ADHD misbehave out of disrespect for rules and class assignments. More than a third of them were uncertain about the role of sugar and food additives in causing ADHD (34.2%). Many (48.8%) classified methylphenidate as a stimulant. More residents reported having sufficient knowledge of ADHD as their time spent in residency increased ($P < 0.05$).
Conclusions: These results identified significant knowledge gaps among the pediatric residents in Lahore, Pakistan, with regard to ADHD. These gaps serve as a barrier toward early recognition of the disorder. Greater emphasis is needed on the provision of screening tools and integration of educational courses on pediatric mental health in the postgraduate curriculum of pediatric residency training in Pakistan. A limitation of the study is the absence of data from the private sector hospitals for comparison. Further studies, including gathering data across the country's urban and rural areas, are needed

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J Am Acad Child Adolesc Psychiatry. 2017;56:S277-S278.

PRESCRIBED MEDICATION AND HEALTH OUTCOMES IN YOUTH WITH OBESITY AND ATTENTION-DEFICIT/HYPERACTIVITY DISORDER (ADHD).

Salter KP, Lim CS, Merideth PT.

Objectives: The relationship between externalizing disorders and pediatric obesity has recently been researched. This study aims to examine the comorbidity of ADHD and pediatric obesity: 1) What is the prevalence of ADHD in an outpatient pediatric obesity medical clinic?; 2) Of those with ADHD, how many are treated pharmacologically?; 3) Are there differences in BMI z-score, heart rate, blood pressure, and hemoglobin A1C among those treated with medication, no medication, and those without ADHD?

Methods: Participants included patients aged 1-18 years (N = 645, mean age = 12.19 years), attending a pediatric obesity clinic (mean BMIz-score = 2.64). Information on the diagnosis of ADHD and medication status was obtained by parent report. To examine differences in health outcomes between groups, ANOVAs was conducted for the health outcomes of interest. Similar methods will be used with electronic health records.
Results: Patients (16.3%) were reported by parents to have ADHD. Per parent report, of those with ADHD, 57.1 percent were medicated for ADHD and 36.2 percent were nonmedicated. Significant group differences were found in heart rate [F(2,534)= 3.68, P = 0.026]; specifically, the ADHD + medication group had significantly higher heart rate [mean (SD) = 92.54 (16.87)] compared with those in the ADHD + nonmedicated group [mean (SD) = 85.11(14.51)] and those without ADHD [mean (SD) = 87.53(13.74)]. No other significant group differences were found. Differences in BMI zscore were approaching significance [F(2,551) = 2.47, P = 0.086]. Resultsextracted from health records will be analyzed to compare and confirm results.
Conclusions: Prevalence of ADHD in this subgroup of children being medically treated for obesity exceeds the typical 5.0 percent prevalence rate. More than half of the patients identified by parents with ADHD were being treated with pharmacotherapy. Resultsof this study revealed few significant differences in health outcomes comparing medicated and nonmedicated patients with ADHD with those without ADHD. Future research should include a larger sample size to increase power and validity and use electronic health records to reduce implicit parental bias regarding diagnosis and medication use

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J Am Acad Child Adolesc Psychiatry. 2017;56:S281.

DASOTRALINE EFFICACY THROUGHOUT THE DAY IN CHILDREN WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER (ADHD): RESULTS OF A PHASE THREE, RANDOMIZED, DOUBLE-BLIND, PLACEBOCONTROLLED STUDY IN A LABORATORY CLASSROOM SETTING.

Goldman R, Childress A, Wigal SB, et al.

Objectives: Dasotraline is a novel dopamine and norepinephrine reuptake inhibitor that provides stable plasma concentrations over 24 hours with oncedaily dosing. This phase 3 study evaluated the efficacy and safety of dasotraline in children with ADHD throughout the day in a laboratory classroom setting.
Methods: Children (aged 6-12 years) meeting DSM-5 criteria for ADHD were randomized to two weeks of dasotraline or placebo (dosed daily at home at approximately 8:00 pm). Following an abbreviated practice day, laboratory classroom evaluations took place at baseline and day 15. The primary endpoint was change from baseline at day 15 in ADHD symptoms as measured by mean Swanson, Kotkin, Agler, M-Flynn, and Pelham Scale Combined Score (SKAMP-CS) obtained from the average of seven assessments collected across the 12-hour laboratory classroom day (12-24 hours post-dose). Secondary endpoints included SKAMP scores throughout the day at individual timepoints from 8:00 am through 8:00 pm (12-24 hours post-dose), and measures of safety and tolerability.
Results: Youth patients (N = 112) comprised the intent-to-treat (ITT) population (mean age = 9.5 years; 68.8% male; 92% completed the study). Dasotraline (4 mg/day) significantly improved mean SKAMP-CS versus placebo ($p < 0.0001$, effect size 0.85) with significant effects persisting throughout the day. Mean SKAMP subscores improved significantly for attention ($p < 0.0001$, effect size 0.81) and deportment ($p < 0.001$, effect size 0.70). Treatmentemergent adverse events were mild or moderate in severity; most frequent were (dasotraline 4 mg/day; placebo): insomnia (19.6%; 3.6%, all terms combined), decreased appetite (10.7%; 3.6%), headache (10.7%; 8.9%), affect lability (8.9%; 7.1%), irritability (5.4%; 3.6%), and perceptual disturbances (5.4%; 0%).
Conclusions: In this 2-week, randomized, double-blind, laboratory classroom study in children with ADHD, dasotraline significantly improved ADHD symptoms (including deportment and attention), compared to placebo, and demonstrated sustained efficacy up to 24 hours post-dose. Most common adverse events were insomnia, decreased appetite, and headache

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J Am Acad Child Adolesc Psychiatry. 2017;56:S281.

DASOTRALINE IN CHILDREN WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER (ADHD): RESULTS OF A RANDOMIZED, DOUBLEBLIND, PLACEBO-CONTROLLED STUDY.

Goldman R, Adler L, Spencer TJ, et al.

Objectives: Dasotraline, a novel dopamine and norepinephrine reuptake inhibitor, provides stable plasma concentrations over 24 hours with once-daily dosing. This study evaluated dasotraline in children aged 6-12 years meeting DSM-5 criteria for ADHD (NCT02428088).

Methods: Patients were randomized to either six weeks of once-daily, fixed-dose dasotraline (2 or 4 mg/day), or placebo. The primary efficacy endpoint was change from baseline (CFB) in ADHD Rating Scale-IV Home Version (ADHD-RS-IV HV) total score at week six, using a mixed model for repeated measures in the intent-to-treat (ITT) population. Secondary endpoints included Clinical Global Impression-Severity (CGI-S) score and safety.

Results: The mean age of 342 randomized patients was 9.1 (1.9) years; 66.7 percent were male. Overall, 79 percent of patients completed the study. In the ITT population (N = 336), ADHD RS-IV HV total score improved significantly with dasotraline 4 mg/day versus placebo [least squares (LS) mean CFB at week 6: -17.53 (95% CI: -20.12, -14.95) vs -11.36 (-13.89, -8.83), respectively, $p < 0.001$; effect size (ES): 0.48]. Inattentiveness and hyperactivity/impulsivity subscale scores significantly improved with 4 mg/day versus placebo at week six ($p = 0.001$, $p = 0.003$, respectively). The 2 mg/day arm did not significantly differ from placebo on ADHD RS-IV HV total score [LS mean CFB at week 6: -11.80 (-14.37, -9.22), $p = 0.812$; ES: 0.03). Improvement in CGI-S score was statistically significant with dasotraline 4 mg/day versus placebo [LS mean CFB at week 6: -1.39 (-1.63, -1.15) vs -1.04 (-1.28, -0.80), respectively, $p = 0.040$; ES: 0.29]. No significant improvement was observed on the CGI-S for dasotraline 2 mg/day versus placebo [LS mean CFB at week 6: -0.94 (-1.18, -0.70), ns]. The most frequent treatment-emergent AEs (5% and higher than placebo) were (2 mg/day; 4 mg/day; placebo): insomnia (15.3%; 21.7%; 4.3%, all terms combined), decreased appetite (12.6%; 21.7%; 5.2%), weight loss (5.4%; 8.7%; 0%), irritability (3.6%; 7.0%; 6.0%), nasopharyngitis (0.9%; 5.2%; 0.9%), and nausea (0%; 5.2%; 2.6%).

Conclusions: Dasotraline 4 mg/day significantly improved ADHD symptoms in children compared to placebo, assessed by ADHD RS-IV HV total score and inattentiveness and hyperactivity/impulsivity subscale scores. Dasotraline was generally well tolerated; most common AEs included insomnia, decreased appetite, weight loss and irritability

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J Am Acad Child Adolesc Psychiatry. 2017;56:S282.

CHALLENGES OF MANAGING ADOLESCENT ATTENTION-DEFICIT/HYPERACTIVITY DISORDER (ADHD) COMORBID WITH SUBSTANCES USE: A REVIEW OF THE LITERATURE.

Goyal D, Parikh T, Pruett JW.

Objectives: Adolescents with ADHD and substance use disorder (SUD) may have an earlier age at onset of SUD. These adolescents may take longer to achieve remission than those with only SUD, who do not have ADHD. They may also likely have a longer course, less desirable outcome, and higher psychiatric comorbidity rate. This review of literature addresses the relationship between ADHD and SUD and potential strategies for identification and treatment of patients with ADHD who are at risk for SUD or have already been diagnosed with comorbid SUD.

Methods: The review of current literature on the topic of comorbid ADHD and SUD was conducted. We searched PubMed and PsycINFO for a 20-year period (June 1997-June 2017). We found 234 initial articles relevant to this search. Thirty articles met the relevance criteria with nine of these being randomized clinical trials, which carry the most evidence-based information.

Results: The literature indicates that adolescents with ADHD have higher risk for developing SUD, as well as a number of other psychiatric disorders. ADHD is more prevalent in patients with SUD, and this complex association pattern is consistent with multiple different substances of abuse. Methylphenidate (MPH) and mixed amphetamine salts (MAS) are the stimulants that are considered first-line pharmacotherapies for ADHD. There is a lower rate of substance use in those who are treated with the medications, including stimulants, despite theoretical potential of abuse of the prescribed stimulants. Of interest, nonstimulant ADHD medications are also noted to be associated with lower SUD. Contradicting studies also exist that report no

change in future SUD even for those treated with medications for ADHD. In addition to abuse of prescription stimulants, specific substances studied per the literature include cigarette smoking, cannabis, and opiate use.
Conclusions: Clinical decisions should be based on a careful analysis of the advantages and disadvantages of pharmacological treatment for ADHD with an individualization of treatment. Some have used the term "precision medicine" for this kind of approach. Psychosocial therapies can also be added to treat both ADHD and SUD. Long term studies on ADHD treatment and substance use are needed

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J Am Acad Child Adolesc Psychiatry. 2017;56:S280.

DOUBLE-BLIND, PLACEBO-CONTROLLED STUDY OF THE NOVEL THERAPEUTIC AEVI-001 IN ADOLESCENTS WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER (ADHD) AND DISRUPTIONS IN GLUTAMATERGIC NETWORK AND NEURONAL CONNECTIVITY GENES.

Findling RL, Anderson C, Fitts D, et al.

Objectives: AEVI-001 is associated with positive effects on learning and memory in animal models. Putative mechanisms include modulation of adenylyl cyclase activity and metabotropic glutamate receptor (GRM) signaling, central cholinergic activity, and g-aminobutyric acidB receptor upregulation. Treatment effects of AEVI-001 were evaluated in adolescents with ADHD and disruptions (copy number variations, CNVs; CNV+ genotype) in glutamatergic network and neuronal connectivity genes [e.g., contactin 4 (CNTN4)].
Methods: Phase 2 randomized, double-blind, placebo-controlled, parallelgroup study of six-week duration was conducted in subjects with ADHD (ages 12-17 years; baseline ADHD-RS-5 score 28 after ADHD medication washout) and CNV+ genotype. Four-week dose optimization was as follows: 100 mg twice daily (BID) starting dose increased weekly based on clinical response to maximal dose of 400 mg BID. Optimized dose (100, 200, or 400 mg BID) was maintained for two weeks. Primary analysis was as follows: a change from baseline ADHD-RS-5 total score at the end of study. Prespecified treatment response was as follows: 30 percent reduction from baseline ADHD-RS-5 total score and/or Clinical Global Impression-Global Improvement score of 1 (very much improved) or 2 (much improved). Post hoc analyses were predictors of treatment response.
Results: Intent-to-treat population included AEVI-001 (n = 49); and placebo (n = 52). Difference between AEVI-001 and placebo was not significant for change from baseline ADHD-RS-5 total score in overall population. Significantly ($P < 0.05$) greater proportion of AEVI-001 subjects met prespecified criteria for clinically meaningful treatment response. Predictors of treatment response were CNVs in certain GRMs and other CNS/neurodevelopmental genes. CNTN4 CNVs most common disruptions in overall study population (19%; AEVI-001, n = 6; placebo, n = 12) and associated with robust response to AEVI-001 (30% reduction in ADHD-RS-5 total score, $P < 0.005$). AEVI-001 was generally well tolerated.
Conclusions: AEVI-001 was associated with a robust efficacy signal in adolescents with ADHD and CNVs in certain GRM and neurodevelopmental genes, particularly CNTN4. Companion study showed that CNTN4 CNV+ subjects with ADHD are at potentially higher risk of poor outcomes with ADHD because of higher prevalence of disruptive behavior, anger control, and risk taking. Further study of this unique population is planned

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J Am Acad Child Adolesc Psychiatry. 2018;57:48-53.

SEXUALLY TRANSMITTED INFECTION AMONG ADOLESCENTS AND YOUNG ADULTS WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER: A NATIONWIDE LONGITUDINAL STUDY.

Chen M-H, Hsu J-W, Huang K-L, et al.

Objective Previous studies have suggested that attention-deficit/hyperactivity disorder (ADHD) is related to risky sexual behaviors, which have been regarded as a major risk factor of sexually transmitted infection (STI). However, the association between ADHD and subsequent STIs remains unknown.
Method Using the Taiwan National Health Insurance Research Database, 17,898 adolescents and young adults who were diagnosed with ADHD by psychiatrists and 71,592 age- and sex-matched comparisons

without ADHD were enrolled from 2001 through 2009 and followed to the end of 2011. Participants who developed any STI during the follow-up period were identified. Cox regression analysis was performed to examine the risk of STIs between patients with ADHD and those without ADHD.
Results Patients with ADHD were prone to developing any STI (hazard ratio [HR] 3.36, 95% CI 2.69Γê+4.21) after adjusting for demographic data, psychiatric comorbidities, and ADHD medications compared with the comparison group. Substance use disorders (HR 1.94, 95% CI 1.27Γê+2.98) also were associated with STI risk. Short-term use (HR 0.70, 95% CI 0.53Γê+0.94) and long-term use (HR 0.59, 95% CI 0.37Γê+0.93) of ADHD medications were related to a lower risk of subsequent STIs. However, an association between substance use disorders and STIs was observed only in women. By contrast, the effect of ADHD medications on the decrease of STI risk was observed only in men.
Conclusion Adolescents and young adults with ADHD had an increased risk of developing any STI later in life compared with the non-ADHD comparisons. Patients with ADHD who also had substance use disorders were at the highest risk of subsequent STIs. Treatment with ADHD medications was associated with a lower risk of subsequent STIs

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J Can Acad Child Adolesc Psychiatry. 2018;27:50-56.
RETURNING TO STIMULANTS IN CHILDREN WITH TREATMENT RESISTANT ADHD: A CASE SERIES.
McLennan JD, Sparshu S.
Objective: To present a case series of children retrialed on stimulants after initial poor stimulant responses given the paucity of information on the usefulness of this strategy.
Methods: Health records from an ADHD medication service were obtained for six children who: (i) were medication nave at service entry; (ii) had trials of at least one stimulant from each stimulant class; (iii) subsequently received a non-stimulant ADHD medication; and, (iv) were then retried on stimulants.
Results: Initial stimulant discontinuation was a function of adverse effects and/or limited symptom improvement. Minimal response and/or adverse effects to non-stimulants contributed to the decision to retry stimulants. Final ADHD symptom ratings by parents and teachers were significantly better than baseline for this cohort. Three were discharged on stimulants, two as monotherapy.
Conclusion: Further study is required to develop evidence-based treatment algorithms for treatment resistant ADHD. Retrying a stimulant may be one option

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J Neurol Sci. 2017;381:924.
DEFICIT OF VISUOSPATIAL MEMORY IN DELAYED RECALL CONDITION IN ADHD CHILDREN.
Kiselev S.
Background: It is known that children with ADHD have deficit in working memory (Martinussen et al, 2012). In our previous research we have revealed that ADHD children have deficit in memory for faces and for names in delayed recall condition (Kiselev & Lvova, 2014; Kiselev & Lvova, 2016). Is it true for visuospatial memory?
Objective: The goal of this research was to examine the hypothesis that ADHD children have deficit in visuospatial memory in delayed recall condition.
Patients and Methods/Material and Methods: The experimental group included 24 ADHD children at age 7-9-years. The control group consisted of 24 typically developing children. The children from experimental and control group were matched for IQ, gender and age. Children from both groups were assessed with visuospatial memory subtest from Luria's neuropsychological assessment battery. It is designed to assess the ability to perform visuospatial memory for 4 geometrical figures in immediate and delayed recall conditions. Twoway ANOVA was used to reveal group differences in reproducing the figures in two conditions.
Results: We have not revealed significant differences between children from experimental and control group in the reproducing the figures in immediate condition. However, the interaction of condition type and group

was significant (0,05). ADHD children were less successful in reproducing the figures in delayed recall condition.
Conclusion: In view of results that we have obtained in our previous researches, it can be assumed that children with ADHD have a specific deficit in memory in delayed recall condition

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J Neurol Sci. 2017;381:189.
RELIABILITY AND VALIDITY OF BACKWARD DIGIT SPAN FOR ELEMENTARY SCHOOL STUDENTS ATTENTION DEFICIT SCREENING AT YOGYAKARTA.
Cempaka Thursina CT.
Background: Attention deficit will bring a serious impact through their future life, so serious attention about the symptoms, children behavior observational, and using attention deficit examination tools precisely will make an earlier care that brings a better prognosis. The reliability and validity of Stroop Test as gold standard examination never been compared with another easier and simpler tools, like Backward Digit Span.
Objective: This study was cross-sectional diagnostic experiment that aimed to compare the reliability and validity of Backward Digit Span Test with Stroop.
Patients and Methods/Material and Methods: Test as gold standard examination in elementary school students near Yogyakarta area. The reliability measured by using coefficient of Cronbach's Alpha and Intraclass Correlation Coefficient (ICC), while the validity measured by 2x2 diagnostic test table to get sensitivity and specificity value then continued by counting Kappa value of this test.
Results: Ninety four subjects joined this study. The coefficient of Cronbach's Alpha was 0.921 and the ICC value was 0,853. This result indicating Backward Digit Span Test have a good reliability. For the first examiner the result was 50 % for each sensitivity and specificity, then for second examiner the sensitivity value was 31, 25% and the specificity was 43 %. Kappa value was 0,000 for the first examiner and-0,026 for the second examiner. The result indicating a low validity of Backward Digit Span.
Conclusion: Backward Digit Span Test had a good reliability with low validity to assess attention deficit of elementary school children

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MMWR Morb Mortal Wkly Rep. 2017 Jan;65:1470-73.
ADVERSE HEALTH EFFECTS ASSOCIATED WITH LIVING IN A FORMER METHAMPHETAMINE DRUG LABORATORY - VICTORIA, AUSTRALIA, 2015.
Wright J, Kenneally ME, Edwards JW, et al.
The manufacture of methamphetamine in clandestine drug laboratories occurs in various locations, including residential houses and apartments. Unlike the controlled manufacture of chemicals and drugs, clandestine manufacture results in the uncontrolled storage, use, generation, and disposal of a wide range of chemicals and the deposit of methamphetamine drug residues on indoor surfaces (1). These residues have been found at high levels on porous and nonporous surfaces and have been shown to persist for months to years (1). Persons exposed to these environments often have poorly defined exposures and health effects. It is commonly assumed that these levels of exposure are low compared with those related to illicit drug use or therapeutic use of amphetamine-based drugs for managing behavioral issues such as attention deficit hyperactivity disorder (2). In 2015, a family that was unknowingly exposed to methamphetamine residues in a house in Australia was found to have adverse health effects and elevated methamphetamine levels in hair samples, highlighting the potential for public health risks for persons who might live in methamphetamine-contaminated dwellings. This case study highlights the importance of the identification and effective decontamination of former clandestine drug laboratories

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MMWR Morb Mortal Wkly Rep. 2018 Jan;67:66-70.

ATTENTION-DEFICIT/HYPERACTIVITY DISORDER MEDICATION PRESCRIPTION CLAIMS AMONG PRIVATELY INSURED WOMEN AGED 15-44 YEARS - UNITED STATES, 2003-2015.

Anderson KN, Ailes EC, Danielson M, et al.

Attention-deficit/hyperactivity disorder (ADHD) is a neurodevelopmental disorder that affects individuals across the lifespan. ADHD medication use among pregnant women is increasing (1), but consensus about the safety of ADHD medication use during pregnancy is lacking. Given that nearly half of U.S. pregnancies are unintended (2), and early pregnancy is a critical period for fetal development, examining trends in ADHD medication prescriptions among reproductive-aged women is important to quantify the population at risk for potential exposure. CDC used the Truven Health MarketScan Commercial Database* for the period 2003-2015 to estimate the percentage of women aged 15-44 years with private employer-sponsored insurance who filled prescriptions for ADHD medications each year. The percentage of reproductive-aged women who filled at least one ADHD medication prescription increased 344% from 2003 (0.9% of women) to 2015 (4.0% of women). In 2015, the most frequently filled medications were mixed amphetamine salts, lisdexamfetamine, and methylphenidate. Prescribing ADHD medications to reproductive-aged women is increasingly common; additional research on ADHD medication safety during pregnancy is warranted to inform women and their health care providers about any potential risks associated with ADHD medication exposure before and during pregnancy

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Mol Psychiatry. 2017 Apr;22:625-33.

CNTN6 MUTATIONS ARE RISK FACTORS FOR ABNORMAL AUDITORY SENSORY PERCEPTION IN AUTISM SPECTRUM DISORDERS.

Mercati O, Huguet G, Danckaert A, et al.

Contactin genes CNTN5 and CNTN6 code for neuronal cell adhesion molecules that promote neurite outgrowth in sensory-motor neuronal pathways. Mutations of CNTN5 and CNTN6 have previously been reported in individuals with autism spectrum disorders (ASDs), but very little is known on their prevalence and clinical impact. In this study, we identified CNTN5 and CNTN6 deleterious variants in individuals with ASD. Among the carriers, a girl with ASD and attention-deficit/hyperactivity disorder was carrying five copies of CNTN5. For CNTN6, both deletions (6/1534 ASD vs 1/8936 controls; P=0.00006) and private coding sequence variants (18/501 ASD vs 535/33480 controls; P=0.0005) were enriched in individuals with ASD. Among the rare CNTN6 variants, two deletions were transmitted by fathers diagnosed with ASD, one stop mutation CNTN6(W923X) was transmitted by a mother to her two sons with ASD and one variant CNTN6(P770L) was found de novo in a boy with ASD. Clinical investigations of the patients carrying CNTN5 or CNTN6 variants showed that they were hypersensitive to sounds (a condition called hyperacusis) and displayed changes in wave latency within the auditory pathway. These results reinforce the hypothesis of abnormal neuronal connectivity in the pathophysiology of ASD and shed new light on the genes that increase risk for abnormal sensory perception in ASD

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Nat Commun. 2018 Jan;9:4.

FASORACETAM IN ADOLESCENTS WITH ADHD AND GLUTAMATERGIC GENE NETWORK VARIANTS DISRUPTING MGLUR NEUROTRANSMITTER SIGNALING.

Elia J, Ungal G, Kao C, et al.

The glutamatergic neurotransmitter system may play an important role in attention-deficit hyperactivity disorder (ADHD). This 5-week, open-label, single-blind, placebo-controlled study reports the safety, pharmacokinetics and responsiveness of the metabotropic glutamate receptor (mGluR) activator fasoracetam (NFC-1), in 30 adolescents, age 12-17 years with ADHD, harboring mutations in mGluR network genes. Mutation status was double-blinded. A single-dose pharmacokinetic profiling from 50-800 mg was followed by a single-blind placebo at week 1 and subsequent symptom-driven dose advancement up to 400 mg BID for 4 weeks. NFC-1 treatment resulted in significant improvement. Mean Clinical Global Impressions-

Improvement (CGI-I) and Severity (CGI-S) scores were, respectively, 3.79 at baseline vs. 2.33 at week 5 (P < 0.001) and 4.83 at baseline vs. 3.86 at week 5 (P < 0.001). Parental Vanderbilt scores showed significant improvement for subjects with mGluR Tier 1 variants (P < 0.035). There were no differences in the incidence of adverse events between placebo week and weeks on active drug. The trial is registered at https://clinicaltrials.gov/ct2/show/study/NCT02286817

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NeuroImage. 2018;169:395-406.

NEURAL CIRCUITRY UNDERLYING SUSTAINED ATTENTION IN HEALTHY ADOLESCENTS AND IN ADHD SYMPTOMATOLOGY.

O'Halloran L, Cao Z, Ruddy K, et al.

Moment-to-moment reaction time variability on tasks of attention, often quantified by intra-individual response variability (IRV), provides a good indication of the degree to which an individual is vulnerable to lapses in sustained attention. Increased IRV is a hallmark of several disorders of attention, including Attention-Deficit/Hyperactivity Disorder (ADHD). Here, task-based fMRI was used to provide the first examination of how average brain activation and functional connectivity patterns in adolescents are related to individual differences in sustained attention as measured by IRV. We computed IRV in a large sample of adolescents (n = 758) across ΓÇÿGoΓÇÖ trials of a Stop Signal Task (SST). A data-driven, multi-step analysis approach was used to identify networks associated with low IRV (i.e., good sustained attention) and high IRV (i.e., poorer sustained attention). Low IRV was associated with greater functional segregation (i.e., stronger negative connectivity) amongst an array of brain networks, particularly between cerebellum and motor, cerebellum and prefrontal, and occipital and motor networks. In contrast, high IRV was associated with stronger positive connectivity within the motor network bilaterally and between motor and parietal, prefrontal, and limbic networks. Consistent with these observations, a separate sample of adolescents exhibiting elevated ADHD symptoms had increased fMRI activation and stronger positive connectivity within the same motor network denoting poorer sustained attention, compared to a matched asymptomatic control sample. With respect to the functional connectivity signature of low IRV, there were no statistically significant differences in networks denoting good sustained attention between the ADHD symptom group and asymptomatic control group. We propose that sustained attentional processes are facilitated by an array of neural networks working together, and provide an empirical account of how the functional role of the cerebellum extends to cognition in adolescents. This work highlights the involvement of motor cortex in the integrity of sustained attention, and suggests that atypically strong connectivity within motor networks characterizes poor attentional capacity in both typically developing and ADHD symptomatic adolescents

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Neuropsychiatr Dis Treat. 2017 Dec;13.

EFFECT OF HANDEDNESS ON AUDITORY ATTENTIONAL PERFORMANCE IN ADHD STUDENTS.

Schmidt SL, Carvaho ALN, Simoes EN.

The relationship between handedness and attentional performance is poorly understood. Continuous performance tests (CPTs) using visual stimuli are commonly used to assess subjects suffering from attention deficit hyperactivity disorder (ADHD). However, auditory CPTs are considered more useful than visual ones to evaluate classroom attentional problems. A previous study reported that there was a significant effect of handedness on students' performance on a visual CPT. Here, we examined whether handedness would also affect CPT performance using only auditory stimuli. From an initial sample of 337 students, 11 matched pairs were selected. Repeated ANOVAs showed a significant effect of handedness on attentional performance that was exhibited even in the control group. Left-handers made more commission errors than right-handers. The results were interpreted considering that the association between ADHD and handedness reflects that consistent left-handers are less lateralized and have decreased interhemispheric connections. Auditory

attentional data suggest that left-handers have problems in the impulsive/hyperactivity domain. In ADHD, clinical therapeutics and rehabilitation must take handedness into account because consistent sinistrals are more impulsive than dextrals

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Neuropsychology. 2017 May;31:448-66.

SPECIFICITY OF EXECUTIVE FUNCTIONING AND PROCESSING SPEED PROBLEMS IN COMMON PSYCHOPATHOLOGY.

Nigg JT, Jester JM, Stavro GM, et al .

OBJECTIVE: Interest continues in neuropsychological measures as cross-disorder intermediate phenotypes in understanding psychopathology. A central question concerns their specificity versus generalizability to particular forms of psychopathology, particularly for executive functioning (EF) and response speed. Three conceptual models examining these relationships were tested to clarify this picture at different levels in the diagnostic hierarchy.

METHOD: Participants (total n = 641, age 18-60) yielded complete structured diagnostic interviews and a neuropsychological test battery comprising measures of executive function, processing speed, and IQ. Repeated measures multivariate analysis of variance, linear regression, and structural equation modeling (SEM) were used to test (a) a specificity model, which proposes that individual disorders are associated with component EF processes and speed; (b) a severity model, which proposes that the total number of comorbid disorders explain poor EF and/or slow speed; and (c) a higher-order dimensional model, which proposes that internalizing versus externalizing disorders are differentially related to EF or speed.

RESULTS: EF effects were best explained by a specificity model, with distinct aspects of EF related to attention deficit hyperactivity disorder versus antisocial substance use disorders. Speed, on the other hand, emerged as a general indicator of externalizing psychopathology in the dimensional model, as well as overall severity of psychopathology in the severity model.

CONCLUSIONS: Granular approaches are likely to be most productive for linking EF to psychopathology, whereas response speed has underused potential as an endophenotype for psychopathology liability. Results are discussed in terms of an integrated conceptualization of neuropsychological processes and putative neural systems involved in general and specific aspects of psychopathology

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NeuroRehabilitation. 2017;40:493-99.

PILOT STUDY OF THE SUB-SYMPTOM THRESHOLD EXERCISE PROGRAM (SSTEP) FOR PERSISTENT CONCUSSION SYMPTOMS IN YOUTH.

Chrisman SPD, Whitlock KB, Somers E, et al.

BACKGROUND: Prior studies suggest potential benefit using monitored aerobic exercise to treat youth with persistent concussion symptoms, but these studies have been small.

OBJECTIVES: To explore the safety and potential benefits of a rehabilitative exercise intervention, the Sub-symptom Threshold Exercise Program (SSTEP), for treating youth with persistent concussion symptoms >1 month.

METHODS: We conducted a retrospective cohort study of 83 youth who participated in SSTEP, completing trajectory analysis of concussion symptoms using the symptom subscale of the Sport Concussion Assessment Tool, version 2 (SCAT-2).

RESULTS: The average age of patients was 14.9+/-2.3 years and 54% were female. Most concussions (76%) were due to sports, the majority from football and girls' soccer, and 55% had a previous concussion. Comorbidity was not uncommon: 14% had history of ADHD and 16% history of depression and/or anxiety. Most patients improved following the intervention, and none reported worsening. Symptoms decreased exponentially following initiation of SSTEP, and trajectory did not differ by duration of symptoms at presentation (<6 weeks, 6-12 weeks, >12 weeks).

CONCLUSIONS: Monitored exercise programs appear to be safe and potentially beneficial for youth with persistent concussive symptoms. Large-scale controlled studies are needed to examine efficacy, ideal timing and duration

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No To Hattatsu. 2015;47:S211.

FNIRS-BASED ASSESSMENT OF MPH EFFECT IN DRUG-NAIVE ADHD : A DOUBLE-BLIND, PLACEBO-CONTROLLED STUDY.

Nagashima M, Monden Y, Dan I, et al.

Objective We have reported reduced right prefrontal cortcx (rPFC) activation in non-medication-naive (non-naive) ADHD children during an inhibition task in an fNIRS study. However, brain function and structure can change with long-Term methylphenidate (MPH! administration. Thus, to establish an objective parameter for successful early diagnosis and treatment, here we assessed the effectiveness of MPH in initial intervention of naive ADHD children.

Method Using fNIRS, we monitored die oxy-Hb changes of 20 right-handed ADHD (mean age, 8.5 years) with IQ>70 performing a go/no-go task before and 1.5 h after MPH or placebo administration, in a randomized, double-blind, placebo-controlled, crossover clinical trial. Twenty age-And gender-matched normal controls (no MPH) were also monitored. Written consent was got from all subjects. The study was authorized by die Ethics Committees.

Results Relative to control subjects, ADHD exhibited rcduced activation in the rPFC ($p<0.05$, Bonferroni corrected) during go/no-go tasks. The reduced rPFC activation was acutely normalized after MPH, but not placebo, administration.

Conclusion MPH normalized inhibitory function in naive ADHD children as evidenced by changes in rPFC activation. This activation could serve as a pharmacological parameter for monitoring acute effects of MPH in naive ADHD children. Thus, fNIRS-based technical applications will contribute to the early objective diagnosis and treatment of ADHD in children

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No To Hattatsu. 2016;48:S237.

FNIRS-BASED ASSESSMENT OF INDIVIDUAL CLASSIFICATION OF ADHD CHILDREN DURING AN INHIBITION TASK.

Nagashima M, Monden Y, Dan I, et al.

Objective-An objective biomarker for the diagnosis of ADHD has not been established. In our previous functional near-infrared spectroscopy(fNIRS)-based studies, we reported reduced right prefrontal cortex activation in ADHD children compared with typically developing(TD) control children during an inhibition task at the group level. The current study aimed to explore a method of individual differentiation between ADHD and TD children.

Methods-Thirty right-handed ADHD children(mean age:9.1 yr., range:6-15 yr.) with IQ>70 and 30 TD age-matched children underwent fNIRS to assess their cortical activation during an inhibition task. We explored specific regions of interest(ROIs) and cut-off amplitudes for cortical activation to distinguish ADHD children from TD children. Written consent was obtained from all subjects. The study was authorized by the applicable ethics committees.

Results-The optimal ROIs were located on the border of the right inferior and middle frontal gyri (IFG-MFG). At the optimal cut-off value of 0.0111 mM-mm, differentiation was achieved with 90% sensitivity and with an area under the curve value of 85%.

Discussion-The fNIRS-based measurements were simple and sufficiently robust, including subjects as young as 6 years. Hypoactivation of the right IFG-MFG assessed by fNIRS during an inhibition task can contribute to the establishment of an effective biomarker for classifying ADHD children at the individual level

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Pain. 2017 Jan;158:140-48.

INCIDENT AND LONG-TERM OPIOID THERAPY AMONG PATIENTS WITH PSYCHIATRIC CONDITIONS AND MEDICATIONS: A NATIONAL STUDY OF COMMERCIAL HEALTH CARE CLAIMS.

Quinn PD, Hur K, Chang Z, et al.

There is growing evidence that opioid prescribing in the United States follows a pattern in which patients who are at the highest risk of adverse outcomes from opioids are more likely to receive long-term opioid therapy. These patients include, in particular, those with substance use disorders (SUDs) and other psychiatric conditions. This study examined health insurance claims among 10,311,961 patients who filled prescriptions for opioids. Specifically, we evaluated how opioid receipt differed among patients with and without a wide range of preexisting psychiatric and behavioral conditions (ie, opioid and nonopioid SUDs, suicide attempts or other self-injury, motor vehicle crashes, and depressive, anxiety, and sleep disorders) and psychoactive medications (ie, antidepressants, benzodiazepines, hypnotics, mood stabilizers, antipsychotics, and medications used for SUD, tobacco cessation, and attention-deficit/hyperactivity disorder). Relative to those without, patients with all assessed psychiatric conditions and medications had modestly greater odds of subsequently filling prescriptions for opioids and, in particular, substantially greater risk of long-term opioid receipt. Increases in risk for long-term opioid receipt in adjusted Cox regressions ranged from approximately 1.5-fold for prior attention-deficit/hyperactivity disorder medication prescriptions (hazard ratio [HR] = 1.53; 95% confidence interval [CI], 1.48-1.58) to approximately 3-fold for prior nonopioid SUD diagnoses (HR = 3.15; 95% CI, 3.06-3.24) and nearly 9-fold for prior opioid use disorder diagnoses (HR = 8.70; 95% CI, 8.20-9.24). In sum, we found evidence of greater opioid receipt among commercially insured patients with a breadth of psychiatric conditions. Future studies assessing behavioral outcomes associated with opioid prescribing should consider preexisting psychiatric conditions

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Pediatr Ann. 2017 Jul;46:e270-e272.

LUCY MAUDE MONTGOMERY AND ANNE OF GREEN GABLES: AN EARLY DESCRIPTION OF ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.

Edison JK, Clardy C.

Attention-deficit/hyperactivity disorder (ADHD) was added to the Diagnostic and Statistical Manual of Mental Disorders, third edition, revised in 1987. Similar disorders had appeared earlier, and many consider the first description of ADHD to be a lecture in 1902 about children with an "abnormal defect in moral control" but normal intelligence. This definition of ADHD is more alarming than the current one. Anne Shirley, the protagonist of the novel Anne of Green Gables (written by Lucy Maude Montgomery and published in 1908), shares the hyperactive and inattentive qualities that fit the current definition of ADHD. She also lacks the menacing characteristics of the 1902 description. This indicates that ADHD, by its modern definition, was probably present in the early 1900s. Furthermore, the character of Anne Shirley shares many biographical similarities with her author, suggesting that Montgomery herself may have had ADHD. Thus, looking at literature from the past not only provides insight into the timeline of ADHD, but also into the thought process of an individual with ADHD. By viewing literary classics through a medical lens, we may gain insight into other diseases as well.

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Pediatr Int. 2017 Feb;59:181-84.

ATOMOXETINE AMELIORATES NOCTURNAL ENURESIS WITH SUBCLINICAL ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.

Ohtomo Y.

BACKGROUND: Recent studies have shown that incontinence and attention-deficit/hyperactivity disorder (ADHD) coexist and there is an interaction between them. The treatment for nocturnal enuresis (NE) and ADHD, however, has not been established. METHODS: At the first visit to the outpatient clinic, physical examination and history taking were carried out in 265 new patients with NE. After excluding the possibility of comorbid ADHD and related disorders, patients with monosymptomatic NE (MNE) were treated with

desmopressin and/or alarm, and those with non-monosymptomatic NE (NMNE) were treated with anti-cholinergics and/or alarm. This 12 week treatment did not work in 65 patients, and they were re-assessed for comorbid ADHD. A total of 24 were diagnosed with ADHD, and they were treated with atomoxetine (1.8 mg/kg/day) in addition to ongoing therapy for NE. RESULTS: After 8 weeks of atomoxetine, the average wet nights per months was significantly decreased: 18.5-4.6 in the MNE group (P = 0.001), and 22.1-12.4 in the NMNE group (P = 0.0251). Overall, atomoxetine was beneficial in 19 of 24 patients. CONCLUSIONS: Atomoxetine may be a suitable option for refractory NE with comorbid ADHD

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Pediatr Int. 2017 Feb;59:218-22.

FACTORS ASSOCIATED WITH INTERNET ADDICTION: CROSS-SECTIONAL STUDY OF TURKISH ADOLESCENTS.

Seyrek S, Cop E, Sinir H, et al.

BACKGROUND: The aim of this study was to investigate the prevalence of Internet addiction (IA), and the relationship between sociodemographic characteristics, depression, anxiety, attention-deficit-hyperactivity disorder (ADHD) symptoms and IA in adolescents.

METHODS: This was a cross-sectional school-based study with a representative sample of 468 students aged 12-17 years at the first trimester of the 2013-2014 academic year. The students were assessed using Young's Internet Addiction Scale, Children's Depression Inventory, Beck Anxiety Inventory, Conners' Parent Rating Scale, Conners' Teacher Rating Scale, Hollingshead-Redlich Scale, and the information form including characteristics of Internet use and socioeconomic status (SES). The relationship between these factors and Internet use was examined.

RESULTS: Approximately 1.6% of students were identified as having IA, whereas 16.2% had possible IA. There were significant correlations between IA and depression, anxiety, attention disorder and hyperactivity symptoms in adolescents. Smoking was also related to IA. There was no significant relationship between IA and age, sex, body mass index, school type, and SES.

CONCLUSIONS: Depression, anxiety, ADHD and smoking addiction are associated with PIU in adolescent students. Preventive public health policies targeting the psychological wellbeing of young people are needed

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Pediatr Int. 2017 Apr;59:416-21.

WHAT HAPPENS TO CHILDREN WHO MOVE OFF THE AUTISM SPECTRUM? CLINICAL FOLLOW-UP STUDY .

Mukaddes NM, Mutluer T, Ayik B, et al.

BACKGROUND: There is controversial information on outcome of school age individuals who lose the diagnosis of autism and achieve "optimal outcome" (OO). The present study assessed the autism symptoms and other psychiatric disorders in a group of children with a past history of autism.

METHODS: The subjects consisted of 26 individuals who had lost the diagnosis of autism 2-8 years previously. Clinical assessment was done with both parents and children. Diagnostic and Statistical Manual of Mental Disorders (5th edn; DSM-V) criteria were used for diagnosis of autism spectrum disorder (ASD). In addition, Childhood Autism Rating Scale and Social Communication Questionnaire (current version) were used. Psychiatric disorders were assessed using the Kiddie Schedule for Affective Disorders and Schizophrenia for School-Age Children Present and Lifetime Version (K-SADS-PL).

RESULTS: None of the participants met the criteria for ASD. Ninety-two percent had a lifetime diagnosis and 81% had a present psychiatric disorder based on the K-SADS. Attention-deficit hyperactivity disorder, specific phobia and obsessive-compulsive disorder were the most common disorders.

CONCLUSIONS: Improved status with regard to autism symptomatology is maintained over time, but these individuals are vulnerable to developing other psychiatric disorders. It is crucial to maintain psychiatric follow up of children who move off the autism spectrum

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Pediatr Neurol. 2017 Apr;69:79-86.

CLINICAL PREDICTORS OF ATTENTION AND EXECUTIVE FUNCTIONING OUTCOMES IN CHILDREN AFTER PERINATAL ARTERIAL ISCHEMIC STROKE.

Bosenbark DD, Krivitzky L, Ichord R, et al.

BACKGROUND: Children with perinatal arterial ischemic stroke (PAIS) are at risk for later neurocognitive and behavioral deficits, yet the clinical predictors of these outcomes are understudied. We examined the influence of clinical and infarct characteristics on attention and executive functioning in children following PAIS.

METHODS: Forty children born at term (>/=37 weeks' gestation) with PAIS (28 with neonatal arterial ischemic stroke and 12 with presumed PAIS) underwent a comprehensive neuropsychological battery at age three to 16 years (median age 7.2 years; 58% male) to assess attention and executive functioning. Parents also completed questionnaires regarding real-world functioning. Clinical variables including perinatal stroke subtype, infarct characteristics (location, laterality, and volume), and the presence of comorbid epilepsy were ascertained from the medical record.

RESULTS: Presumed PAIS, larger infarct volume, and comorbid epilepsy negatively influenced the performance on attention and executive functioning measures. These clinical variables were also associated with greater functional problems on parent reports, including a higher frequency of attention-deficit/hyperactivity disorder symptoms and greater difficulties in some subdomains of executive functioning. Infarct location and laterality were not associated with performance measures or parental report of functioning.

CONCLUSION: Although all children with PAIS are at risk for later deficits in attention and executive functioning, those with presumed PAIS, larger infarct size, and comorbid epilepsy appear to be the most vulnerable. As they approach and reach school age, these children should undergo neuropsychological assessment to ensure timely implementation of therapeutic interventions and behavioral strategies

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Pediatr Neurol. 2017 Jan;66:96-99.

TRANSIENT ISOLATED LOWER BULBAR PALSY WITH ELEVATED SERUM ANTI-GM1 AND ANTI-GD1B ANTIBODIES During Aripiprazole Treatment.

Han TH, Kim DY, Park DW, et al.

BACKGROUND: Transient bulbar palsy without involvement of the facial or extraocular muscles is a rare presentation. It is considered a form of cranial polyneuropathy, a variant of Guillain-Barre syndrome that is related to the autoimmune mechanisms induced by preceding infections or vaccinations. However, drug-induced cranial polyneuropathy has not previously been reported. We describe a boy with isolated bulbar palsy and positive serum antiganglioside antibodies during aripiprazole treatment.

PATIENT DESCRIPTION: This 12-year-old boy was admitted with a seven-day history of dysarthria, tongue discomfort, and tinnitus. Three weeks before symptom onset, aripiprazole was added to the patient's medications for attention-deficit hyperactivity disorder. On examination, he showed curtaining of the pharyngeal wall, tongue fasciculation and deviation, and a weak gag reflex. Cranial magnetic resonance imaging suggested lower cranial nerve involvement. Serum anti-GM1 IgG and anti-GD1b IgG antibodies were positive. After stopping aripiprazole, his bulbar symptoms improved. However, on readministration of aripiprazole seven weeks later, dysarthria recurred and again resolved after stopping the drug.

CONCLUSION: We describe the first patient with anti-GM1 IgG and anti-GD1b IgG antibodies-associated transient cranial polyneuropathy presenting as isolated bulbar palsy. These findings could be an adverse effect of aripiprazole treatment

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Pediatr Drugs. 2017;1.

CORRECTION TO: DEVELOPMENT OF GUANFACINE EXTENDED-RELEASE DOSING STRATEGIES IN CHILDREN AND ADOLESCENTS WITH ADHD USING A PHYSIOLOGICALLY BASED PHARMACOKINETIC MODEL TO PREDICT DRUG-DRUG INTERACTIONS WITH MODERATE CYP3A4 INHIBITORS OR INDUCERS.

Li A, Yeo K, Welty D, et al.

The article Development of Guanfacine Extended-Release Dosing Strategies in Children and Adolescents with ADHD Using a PhysiologicallyBased Pharmacokinetic Model to Predict Drug-Drug Interactions with Moderate CYP3A4 Inhibitors or Inducers, written by Aiqun Li, Karen Yeo, Devin Welty, Haojing Rong, was originally published electronically on the publisher's internet portal (currently SpringerLink) on 02nd November, 2017 without open access

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Pediatrics. 2018;141.

PRENATAL PATERNAL SELECTIVE SEROTONIN REUPTAKE INHIBITORS USE AND RISK OF ADHD IN OFFSPRING.

Yang F, Liang H, Chen J, et al.

Objectives: It has been shown that maternal prenatal exposure to selective serotonin reuptake inhibitors (SSRIs) may be a risk factor for attention-deficit/hyperactivity disorder (ADHD) in offspring. Our goal was to examine whether paternal SSRI use before conception increases the risk of ADHD in offspring.

Methods: On the basis of Danish national registers, we conducted a cohort study of 781 470 singletons born between 1996 and 2008 with follow-up throughout 2013. The children whose fathers used SSRIs during the last 3 months before conception were identified as the exposed. Cox regression was used to estimate the hazard ratio (HR) of ADHD.

Results: A total of 7216 children (0.92%) were born to fathers who had used SSRIs during the last 3 months before conception. There were 12 520 children diagnosed with ADHD. Compared with unexposed children, the exposed had a 26% increased risk of ADHD (HR = 1.26, 95% confidence interval [CI]: 1.06-1.51) after adjusting for potential confounders. When extending the exposure window to 1 year before conception, paternal use of SSRIs only during the period of 12 to 3 months before conception was associated with the HR of 1.35 (95% CI: 1.10-1.66), whereas paternal use of SSRIs only during the last 3 months before conception was associated with a similarly increased risk of ADHD (adjusted HR = 1.31, 95% CI: 0.95-1.82).

Conclusions: The mildly increased risk of ADHD in offspring associated with paternal SSRI use before conception could probably be due to the underlying indications related to SSRI use

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Pediatrics. 2018;141.

ATTENTION-DEFICIT/HYPERACTIVITY DISORDER AND VERY PRETERM/VERY LOW BIRTH WEIGHT: A META-ANALYSIS.

Franz AP, Bolat GU, Bolat H, et al.

Context: Although very preterm (VP), extremely preterm (EP), very low birth weight (VLBW), and extremely low birth weight (ELBW) newborns seem to have a higher risk of later attention-deficit/hyperactivity disorder (ADHD), the magnitude of the risk is not well-defined.

Objective: To systematically review and meta-analyze the risk of VP/VLBW and EP/ELBW individuals to develop a ADHD categorical diagnosis or dimensional symptomatology compared with controls with normal weight and/or birth age.

Data Sources: We used PsycINFO, Medline, Embase, and Cochrane databases.

Study Selection: We selected cross-sectional, prospective, or retrospective studies with no time or language restriction.

Data Extraction: Independent reviewers screened and extracted data using predefined standard procedures.

Results: In 12 studies (N = 1787), researchers relying on a categorical diagnosis showed that both VP/VLBW and EP/ELBW subjects have a higher ADHD risk (odds ratio [OR] = 3.04 higher than controls; 95% confidence interval [CI] 2.19 to 4.21). In subgroup analyses, we demonstrated that the more extreme the cases, the higher the ORs (VP/VLBW: OR = 2.25 [95% CI 1.56 to 3.26]; EP/ELBW: OR = 4.05 [95% CI 2.38

to 6.87]). We drew data from 29 studies (N = 3504) on ADHD symptomatology and found significant associations with inattention (standardized mean difference [SMD] = 1.31, 95% CI 0.66 to 1.96), hyperactivity and impulsivity (SMD = 0.74, 95% CI 0.35 to 1.13), and combined symptoms (SMD = 0.55, 95% CI 0.42 to 0.68) when compared with controls.
Limitations: Heterogeneity was significantly high for all analyses involving the 3 ADHD dimensions.
Conclusions: With our results, we provide evidence that VP/VLBW subjects have an increased risk of ADHD diagnosis and symptomatology compared with controls, and these findings are even stronger in the EP/ELBW group. Future researchers should address which risk factors related to prematurity or low birth weight lead to ADHD

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Pediatrics. 2018;141.
ADHD AND EARLY EXPERIENCE: REVISITING THE CASE OF LOW BIRTH WEIGHT.
Nigg JT, Song M.

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PLoS ONE. 2017;12:e0190248.
MATERNAL DEPRESSIVE SYMPTOMS DURING AND AFTER PREGNANCY ARE ASSOCIATED WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER SYMPTOMS IN THEIR 3- TO 6-YEAR-OLD CHILDREN.
Wolford E, Lahti M, Tuovinen S, et al.
Maternal depressive symptoms during pregnancy have been associated with child behavioural symptoms of attention-deficit/hyperactivity disorder (ADHD) in early childhood. However, it remains unclear if depressive symptoms throughout pregnancy are more harmful to the child than depressive symptoms only during certain times, and if maternal depressive symptoms after pregnancy add to or mediate any prenatal effects. 1,779 mother-child dyads participated in the Prediction and Prevention of Pre-eclampsia and Intrauterine Growth Restriction (PREDO) study. Mothers filled in the Center of Epidemiological Studies Depression Scale biweekly from 12+0-13+6 to 38+0-39+6 weeks+days of gestation or delivery, and the Beck Depression Inventory-II and the Conners' Hyperactivity Index at the child's age of 3 to 6 years (mean 3.8 years, standard deviation [SD] 0.5). Maternal depressive symptoms were highly stable throughout pregnancy, and children of mothers with consistently high depressive symptoms showed higher average levels (mean difference = 0.46 SD units, 95% Confidence Interval [CI] 0.36, 0.56, $p < 0.001$ compared to the low group), and proportion (32.1% vs. 14.7%) and odds (odds ratio = 2.80, 95% CI 2.20, 3.57, $p < 0.001$) of clinically significant ADHD symptoms. These associations were not explained by the effects of maternal depressive symptoms after pregnancy, which both added to and partially mediated the prenatal effects. Maternal depressive symptoms throughout pregnancy are associated with increased ADHD symptomatology in young children. Maternal depressive symptoms after pregnancy add to, but only partially mediate, the prenatal effects. Preventive interventions suited for the pregnancy period may benefit both maternal and offspring mental health

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PLoS ONE. 2017;12:e0188785.
MENTAL HEALTH, BEHAVIOURAL PROBLEMS AND TREATMENT SEEKING AMONG STUDENTS COMMENCING UNIVERSITY IN NORTHERN IRELAND.
McLafferty M, Lapsley CR, Ennis E, et al.
Mental health and behavioural problems are common among students commencing university. University life can be stressful and problems often exacerbate during their course of study, while others develop disorders for the first time. The WHO World Mental Health Surveys International College Student Project aims to conduct longitudinal research to examine and monitor student mental health and wellbeing. The Ulster University Student Wellbeing study, which commenced in September 2015 in Northern Ireland (NI), was conducted as part of this initiative (wave 1, n = 739), using the WMH-CIDI to examine psychopathology. Baseline prevalence rates of lifetime and 12-month mental health and substance disorders, ADHD and

suicidality were high, with more than half of new undergraduate students reporting any lifetime disorder. Co-morbidity was common with 19.1% of students experiencing three or more disorders. Logistic regression models revealed that females, those over 21, non-heterosexual students, and those from a lower SES background were more likely to have a range of mental health and behavioural problems. Overall, 10% of new entry students received treatment for emotional problems in the previous year. However, 22.3% of students with problems said they would not seek help. The study provides important information for universities, policy makers and practice, on mental health and wellbeing in young people generally but particularly for students commencing university. The findings will assist in the development and implementation of protection and prevention strategies in the university setting and beyond

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PLoS ONE. 2018;13:e0189749.

PROOF-OF-CONCEPT STUDY OF AN AT-HOME, ENGAGING, DIGITAL INTERVENTION FOR PEDIATRIC ADHD.

Davis NO, Bower J, Kollins SH.

OBJECTIVE: Pharmacological and behavioral therapies have limited impact on the distinct neurocognitive impairments associated with ADHD, and existing cognitive training programs have shown limited efficacy. This proof-of-concept study assessed treatment acceptability and explored outcomes for a novel digital treatment targeting cognitive processes implicated in ADHD.

METHOD: Participants included 40 children with ADHD and 40 children without ADHD. Following psychiatric screening, ADHD ratings, and baseline neuropsychological measures, participants completed 28-days of at-home treatment. Neuropsychological assessment was repeated at end-of-study along with treatment satisfaction measures.

RESULTS: Eighty-four percent of treatment sessions were completed and ratings showed strong intervention appeal. Significant improvements were observed on a computerized attention task for the ADHD group and a highly impaired ADHD High Severity subgroup. There was no change for the non-ADHD group. Spatial working memory also improved for the ADHD group and the ADHD High Severity subgroup.

CONCLUSION: Findings provide preliminary support that this treatment may improve attention, working memory, and inhibition in children with ADHD. Future research requires larger-scale randomized controlled trials that also evaluate treatment impact on functional impairments.

TRIAL REGISTRATION: ClinicalTrials.gov NCT01943539

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Postgrad Med. 2018 Jan;130:111-21.

EFFECTS OF SHP465 MIXED AMPHETAMINE SALTS IN ADULTS WITH ADHD IN A SIMULATED ADULT WORKPLACE ENVIRONMENT.

Wigal T, Childress A, Frick G, et al.

OBJECTIVES: Evaluate the efficacy, duration of effect, and safety of 25 mg SHP465 mixed amphetamine salts (MAS) extended-release versus placebo in adults with attention-deficit/hyperactivity disorder (ADHD).

METHODS: Adults (18-55 years) with ADHD and with ADHD Rating Scale-IV (ADHD-RS-IV) scores >/=24 were randomized to treatment in a double-blind, 2-period, 2-treatment crossover study utilizing the Adult Workplace Environment (AWE), as described by Wigal and Wigal (J Atten Disord 2006;10:92-111). On day 7 of each 7-day treatment period, efficacy was assessed during a 16.5-hour postdose period. The primary endpoint, Permanent Product Measure of Performance (PERMP) total score, was analyzed in the intent-to-treat population using a mixed linear model of analysis of variance. Secondary endpoints, for which the study was not powered, included PERMP problems attempted and answered correctly, ADHD clinician ratings based on counselor observations and inputs during the Time Segment Rating System (Co-ADHD-RS TSRS), and the ADHD self-rating scale (ADHD-SRS). Safety and tolerability assessments included treatment-emergent adverse events (TEAEs) and vital signs.

RESULTS: The least squares mean (95% CI) treatment difference (SHP465 MAS-placebo) for PERMP total score significantly favored SHP465 MAS over placebo when averaged across all postdose assessments (19.29 [10.95, 27.63]; P < 0.0001), with significant treatment differences favoring SHP465 MAS over placebo

observed at 4-16 hours postdose (all P < 0.01). TEAEs observed with SHP465 MAS (>/=5% of participants) included insomnia, decreased appetite, dry mouth, headache, and anorexia. Mean pulse and blood pressure increases with SHP465 MAS exceeded those of placebo.
CONCLUSIONS: SHP465 MAS (25 mg) was superior to placebo on PERMP total score, with treatment differences observed from 4 to 16 hours postdose; nominal treatment differences on the ADHD-SRS, but not the Co-ADHD-RS TSRS, were also observed. The safety and tolerability profile of SHP465 MAS was similar to previous reports for SHP465 MAS and other long-acting stimulants.
Clinical trials registry: clinicaltrials.gov (NCT00202605; https://clinicaltrials.gov/ct2/show/NCT00202605)

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Prev Sci. 2017 Apr;18:305-11.
TREATMENT EFFECTS OF A PRIMARY CARE INTERVENTION ON PARENTING BEHAVIORS: SOMETIMES IT'S RELATIVE.
Shaffer A, Lindhiem O, Kolko D.
The goal of this brief report is to demonstrate the utility of quantifying parental discipline practices as relative frequencies in measuring changes in parenting behavior and relations to child behavior following intervention. We explored comparisons across methodological approaches of assessing parenting behavior via absolute and relative frequencies in measuring improvements in parent-reported disciplinary practices (increases in positive parenting practices in response to child behavior; decreases in inconsistent discipline and use of corporal punishment) and child behavior problems. The current study was conducted as part of a larger clinical trial to evaluate the efficacy of a collaborative care intervention for behavior problems, ADHD, and anxiety in pediatric primary care practices (Doctor Office Collaborative Care; DOCC). Participants were 321 parent-child dyads (M child age = 8.00, 65 % male children) from eight pediatric practices that were cluster randomized to DOCC or enhanced usual care (EUC). Parents reported on their own discipline behaviors and child behavior problems. While treatment-related decreases in negative parenting were found using both the absolute and relative frequencies of parenting behaviors, results were different for positive parenting behaviors, which showed decreases when measured as absolute frequencies but increases when measured as relative frequencies. In addition, positive parenting was negatively correlated with child behavior problems when using relative frequencies, but not absolute frequencies, and relative frequencies of positive parenting mediated relations between treatment condition and outcomes. Our findings indicate that the methods used to measure treatment-related change warrant careful consideration

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Psychiatry Res. 2017 Jun;252:234-41.
NEURODEVELOPMENTAL DISORDERS IN YOUNG VIOLENT OFFENDERS: OVERLAP AND BACKGROUND CHARACTERISTICS.
Billstedt E, Anckarsater H, Wallinius M, et al.
Neurodevelopmental disorders (Attention-Deficit/Hyperactivity Disorder (ADHD), Autism Spectrum Disorder (ASD), tic disorder, intellectual disability (ID)), in prison populations have received increased attention but the focus has generally been on one single condition leaving out the global picture. This study assessed the prevalence and overlap of neurodevelopmental disorders (NDD) in a consecutive cohort (n=270) of young adult male offenders (age 18-25 years), sentenced for "hands-on" violent offences and serving prison time in Swedish prisons. Seventy-one percent of all who met inclusion criteria participated. Comprehensive clinical assessments were carried out including history of early antisocial behavior and maladjustment, self-report questionnaires and an intelligence test. Sixty-three percent of the study group met DSM-IV criteria for childhood ADHD, 43% for ADHD in adulthood, 10% met criteria for an ASD, 6% for Tourette syndrome, and 1% for ID. Twenty-two percent had borderline intellectual functioning. A substantial rate of overlap between the NDDs was found. The combined NDD group had an earlier onset of antisocial behavior, had more aggressive behavior and lower school achievements than the non-NDD group. The results highlight the need for prison and probation services to be attentive of and screen for neurodevelopmental disorders in young violent offenders

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Psychiatry Res. 2017 Jul;253:351-59.

TAXOMETRIC ANALYSES AND PREDICTIVE ACCURACY OF CALLOUS-UNEMOTIONAL TRAITS REGARDING QUALITY OF LIFE AND BEHAVIOR PROBLEMS IN NON-CONDUCT DISORDER DIAGNOSES.

Herpers PCM, Klip H, Rommelse NNJ, et al.

Callous-unemotional (CU) traits have mainly been studied in relation to conduct disorder (CD), but can also occur in other disorder groups. However, it is unclear whether there is a clinically relevant cut-off value of levels of CU traits in predicting reduced quality of life (QoL) and clinical symptoms, and whether CU traits better fit a categorical (taxonic) or dimensional model. Parents of 979 youths referred to a child and adolescent psychiatric clinic rated their child's CU traits on the Inventory of Callous-Unemotional traits (ICU), QoL on the Kidscreen-27, and clinical symptoms on the Child Behavior Checklist. Experienced clinicians conferred DSM-IV-TR diagnoses of ADHD, ASD, anxiety/mood disorders and DBD-NOS/ODD. The ICU was also used to score the DSM-5 specifier 'with limited prosocial emotions' (LPE) of Conduct Disorder. Receiver operating characteristic (ROC) analyses revealed that the predictive accuracy of the ICU and LPE regarding QoL and clinical symptoms was poor to fair, and similar across diagnoses. A clinical cut-off point could not be defined. Taxometric analyses suggested that callous-unemotional traits on the ICU best reflect a dimension rather than taxon. More research is needed on the impact of CU traits on the functional adaptation, course, and response to treatment of non-CD conditions

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Psychiatry Res. 2017 Jun;252:185-87.

ASSOCIATION OF Y-LINKED VARIANTS WITH IMPULSIVITY AND AGGRESSION IN BOYS WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER OF CHINESE HAN DESCENT.

Liu L, Cheng J, Li H, et al.

Y chromosome plays important role in brain function and may help to explain the sex difference in attention-deficit/hyperactivity disorder (ADHD). A total of 857 boys with ADHD and 574 male controls were genotyped for 14 Y-linked markers. Analyses for both dichotomous phenotype and quantitative traits and the interaction effects with MAOA were performed. The results indicated significant association of four markers (M88, M95, M175, and M119) with inhibition function and aggression in boys with ADHD. Positive interaction effects with MAOA were also detected. In conclusion, some Y-linked variants may be associated with the impulsivity and aggression in boys with ADHD

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Psychiatry Res. 2018;261:40-44.

EVALUATION OF MOTOR PROFICIENCY AND ADIPONECTIN IN ADOLESCENT STUDENTS WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER AFTER HIGH-INTENSITY INTERMITTENT TRAINING.

Torabi F, Farahani A, Safakish S, et al.

Attention deficit hyperactivity disorder (ADHD) is a chronic condition with frequent comorbidities such as obesity, troubled relationships, low self-esteem, and difficulty in motor proficiency. This study aims to elucidate the effect of high-intensity intermittent training on motor proficiency, adiponectin, and insulin resistance in adolescent students with ADHD disorder. Fifty adolescent students of both genders with ADHD diagnosis participated and assigned into four experimental groups (each group with 15 girls and 10 boys students; two experimental and two control groups). High-intensity intermittent training was performed continuously 3 times a week for 6 weeks in experimental groups. Serum adiponectin level significantly increased in the experimental groups of both genders after 6 weeks intermittent training while insulin resistance levels were markedly decreased. Furthermore, motor proficiency score were significantly improved in the experimental groups of both genders. In addition gender had no significant impact on adiponectin, insulin resistance and motor proficiency rating. The findings of this study suggest that high intensity intermittent training improved physiological systems in ADHD population that leads to reduce risk factors for future development of comorbidities

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Psychiatry Res. 2018;261:212-19.

SERUM LEVELS OF CORTISOL, DEHYDROEPIANDROSTERONE, AND OXYTOCIN IN CHILDREN WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER COMBINED PRESENTATION WITH AND WITHOUT COMORBID CONDUCT DISORDER.

Toker A, et al.

The present study aimed to investigate serum cortisol, dehydroepiandrosterone (DHEA), and oxytocin levels of children with attention-deficit/hyperactivity disorder (ADHD) combined presentation and those diagnosed with ADHD combined presentation and coexisting conduct disorder. A total of 74 drug-naive children with ADHD combined presentation alone, 32 children with ADHD combined presentation + conduct disorder, and 42 healthy controls were included. The severities of ADHD and conduct disorder symptoms were assessed via parent- and teacher-rated questionnaires. The severity of aggression, anxiety, and depression symptoms of the children were assessed by the self-report inventories. Independent of potential confounders, including age, sex, pubertal stage, and severity of depression and anxiety, serum oxytocin levels of the ADHD combined presentation + conduct disorder group were significantly lower than those of both the ADHD combined presentation alone and control groups. There was also a trend for the ADHD combined presentation + conduct disorder group to show lower serum DHEA levels than that of the ADHD combined presentation alone group. However, serum cortisol levels did not show significant alterations among the groups. These findings suggest that oxytocin and DHEA may play a role in the pathophysiology of conduct disorder, at least in the presence of ADHD combined presentation

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Psychol Addict Behav. 2017 May;31:307-14.

WHEN ALCOHOL IS ONLY PART OF THE PROBLEM: AN EVENT-LEVEL ANALYSIS OF NEGATIVE CONSEQUENCES RELATED TO ALCOHOL AND OTHER SUBSTANCE USE.

Mallett KA, Turrisi R, Hultgren BA, et al.

While alcohol remains the drug of choice for most college students, national data show that 40% of college students also use other substances (e.g., marijuana, cocaine, etc.). Longitudinal studies indicate that students who report use of both alcohol and other substances experience more consequences (e.g., blackout, arrests). The current study expands upon this research by using a multilevel approach to examine average and event-level alcohol combined with other substance use (ALC+) and its role on consequences experienced. In addition, the research examined which substance combined with alcohol posed the most risk. A total of 461 students reported on alcohol use, substance use, and consequences experienced (e.g., Young Adult Alcohol Consequences Questionnaire [YAACQ]) on 12 weekend nights (Thursday, Friday, Saturday) across 4 weekends in an academic year. Multilevel model analyses revealed a positive association between both average and event-level ALC+ use and the number of consequences experienced. A significant cross-level interaction was also revealed indicating students who typically combine alcohol and other substances experienced more consequences on occasions when they use more substances relative to students who typically use alcohol only. Finally, alcohol plus nicotine, or marijuana, or attention-deficit/hyperactivity disorder (ADHD) medications, or cocaine were all significantly positively related to increased consequences. These findings provide consistent evidence that ALC+ use is a highly prevalent behavior among college students that increases risk of problematic consequences

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Psychol Med. 2017 Jan;47:377-88.

MISMATCH NEGATIVITY AND P3A AMPLITUDE IN YOUNG ADOLESCENTS WITH FIRST-EPISODE PSYCHOSIS: A COMPARISON WITH ADHD.

Rydkjaer J, Mollegaard Jepsen JR, Pagsberg AK, et al.

BACKGROUND: Deficient mismatch negativity (MMN) has been proposed as a candidate biomarker in schizophrenia and may therefore be potentially useful in early identification and intervention in early onset psychosis. In this study we explored whether deficits in the automatic orienting and reorienting responses, measured as MMN and P3a amplitude, are present in young adolescents with first-episode psychosis (FEP)

and whether findings are specific to psychosis compared to young adolescents with attention deficit hyperactivity disorder (ADHD).
METHOD: MMN and P3a amplitude were assessed in young adolescents (age 12-17 years) with either FEP (N = 27) or ADHD (N = 28) and age- and gender-matched healthy controls (N = 43). The MMN paradigm consisted of a four-tone auditory oddball task with deviant stimuli based on frequency, duration and their combination.
RESULTS: Significantly less MMN was found in patients with psychosis compared to healthy controls in response to frequency and duration deviants. MMN amplitudes in the group of patients with ADHD were not significantly different from patients with psychosis or healthy controls. No significant group differences were found on P3a amplitude.
CONCLUSION: Young adolescents with FEP showed impaired MMN compared to healthy controls while intermediate and overlapping levels of MMN were observed in adolescents with ADHD. The findings suggest that young FEP patients already exhibit pre-attentive deficits that are characteristic of schizophrenia albeit expressed on a continuum shared with other neuropsychiatric disorders

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Psychol Med. 2017 Jan;47:353-62.

PRENATAL EXPOSURE TO VERY SEVERE MATERNAL OBESITY IS ASSOCIATED WITH ADVERSE NEUROPSYCHIATRIC OUTCOMES IN CHILDREN.

Mina TH, Lahti M, Drake AJ, et al.

BACKGROUND: Prenatal maternal obesity has been linked to adverse childhood neuropsychiatric outcomes, including increased symptoms of attention deficit hyperactivity disorder (ADHD), internalizing and externalizing problems, affective disorders and neurodevelopmental problems but few studies have studied neuropsychiatric outcomes among offspring born to very severely obese women or assessed potential familial confounding by maternal psychological distress.
METHOD: We evaluated neuropsychiatric symptoms in 112 children aged 3-5 years whose mothers had participated in a longitudinal study of obesity in pregnancy (50 very severe obesity, BMI 40 kg/m2, obese class III and 62 lean, BMI 18.5-25 kg/m2). The mothers completed the Conners' Hyperactivity Scale, Early Symptomatic Syndrome Eliciting Neurodevelopmental Clinical Examination Questionnaire (ESSENCE-Q), Child's Sleep Habits Questionnaire (CSHQ), Strengths and Difficulties Questionnaire (SDQ), and Child Behavior Checklist (CBCL) to assess child neuropsychiatric symptoms. Covariates included child's sex, age, birthweight, gestational age, socioeconomic deprivation levels, maternal age, parity, smoking status during pregnancy, gestational diabetes and maternal concurrent symptoms of anxiety and depression assessed using State Anxiety of Spielberger State-Trait Anxiety Index (STAI) and General Health Questionnaire (GHQ), respectively.
RESULTS: Children exposed to prenatal maternal very severe obesity had significantly higher scores in the Conners' Hyperactivity Scale; ESSENCE-Q; total sleep problems in CSHQ; hyperactivity, conduct problems and total difficulties scales of the SDQ; higher externalizing and total problems, anxious/depressed, aggressive behaviour and other problem syndrome scores and higher DSM-oriented affective, anxiety and ADHD problems in CBCL. Prenatal maternal very severe obesity remained a significant predictor of child neuropsychiatric problems across multiple scales independent of demographic factors, prenatal factors and maternal concurrent symptoms of anxiety and depression.
CONCLUSIONS: Prenatal maternal very severe obesity is a strong predictor of increased neuropsychiatric problems in early childhood

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Psychol Med. 2017 Jan;47:317-25.

CHILDHOOD ATOPY AND MENTAL HEALTH: A PROSPECTIVE, LONGITUDINAL INVESTIGATION.

Goodwin RD, Robinson M, Sly PD, et al.

BACKGROUND: Prior studies have suggested a relationship between atopy and mental health, although methodological barriers have limited the generalizability of these findings. The objective of this study was to

investigate the relationship between early-life atopy and vulnerability to mental health problems among youth in the community.
METHOD: Data were drawn from the Raine Study (N = 2868), a population-based birth cohort study in Western Australia. Logistic regression and generalized estimating equations were used to examine the relationship between atopy at ages 1-5 years [using parent report and objective biological confirmation (sera IgE)], and the range of internalizing and externalizing mental health problems at ages 5-17 years.
RESULTS: Atopy appears to be associated with increased vulnerability to affective and anxiety problems, compared to youth without atopy. These associations remained significant after adjusting for a range of potential confounders. No relationship was evident between atopy and attention deficit hyperactivity disorder or externalizing problems.
CONCLUSIONS: Findings are the first linking atopy (measured by both parent report and objective verification) with increased vulnerability to affective and anxiety problems. Therefore, replication is required. If replicated, future research aimed at understanding the possible biological and/or social and environmental pathways underlying these links is needed. Such information could shed light on shared pathways that could lead to more effective treatments for both atopy and internalizing mental health problems

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Psychol Med. 2017 Apr;47:1126-37.

THE PREDICTORS OF PERSISTENT DSM-IV DISORDERS IN 3-YEAR FOLLOW-UPS OF THE BRITISH CHILD AND ADOLESCENT MENTAL HEALTH SURVEYS 1999 AND 2004.

Ford T, Macdiarmid F, Russell AE, et al.

BACKGROUND: The identification of the factors that influence the persistence of psychiatric disorder may assist practitioners to focus on young people who are particularly prone to poor outcomes, but population-based samples of sufficient size are rare.
METHOD: This secondary analysis combined data from two large, population-based cross-sectional surveys in Great Britain (1999 and 2004) and their respective follow-ups (2002 and 2007), to study homotypic persistence among the 998 school-age children with psychiatric disorder at baseline. Psychiatric disorder was measured using the Development and Well-Being Assessment applying DSM-IV criteria. Factors relating to the child, family, and the severity and type of psychopathology at baseline were analysed using logistic regression.
RESULTS: Approximately 50% of children with at least one psychiatric disorder were assigned the same diagnostic grouping at 3-year follow-up. Persistent attention-deficit/hyperactivity disorder and anxiety were predicted by poor peer relationship scores. Persistent conduct disorder was predicted by intellectual disability, rented housing, large family size, poor family function and by severer baseline psychopathology scores.
CONCLUSIONS: Homotypic persistence was predicted by different factors for different groups of psychiatric disorders. Experimental research in clinical samples should explore whether these factors also influence response to interventions

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Psychol Med. 2017 Jan;47:255-66.

POOR STIMULUS DISCRIMINABILITY AS A COMMON NEUROPSYCHOLOGICAL DEFICIT BETWEEN ADHD AND READING ABILITY IN YOUNG CHILDREN: A MODERATED MEDIATION MODEL.

Lucio PS, Salum GA, Rohde LA, et al.

BACKGROUND: Attention deficit hyperactivity disorder (ADHD) is frequently associated with poorer reading ability; however, the specific neuropsychological domains linking this co-occurrence remain unclear. This study evaluates information-processing characteristics as possible neuropsychological links between ADHD symptoms and RA in a community-based sample of children and early adolescents with normal IQ (70).
METHOD: The participants (n = 1857, aged 6-15 years, 47% female) were evaluated for reading ability (reading single words aloud) and information processing [stimulus discriminability in the two-choice reaction-time task estimated using diffusion models]. ADHD symptoms were ascertained through informant (parent)

report using the Development and Well-Being Assessment (DAWBA). Verbal working memory (VWM; digit span backwards), visuospatial working memory (VSWM, Corsi Blocks backwards), sex, socioeconomic status, and IQ were included as covariates.
RESULTS: In a moderated mediation model, stimulus discriminability mediated the effect of ADHD on reading ability. This indirect effect was moderated by age such that a larger effect was seen among younger children.
CONCLUSION: The findings support the hypothesis that ADHD and reading ability are linked among young children via a neuropsychological deficit related to stimulus discriminability. Early interventions targeting stimulus discriminability might improve symptoms of inattention/hyperactivity and reading ability

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Qual Life Res. 2017 May;26:1283-94.
QUALITY OF LIFE, PSYCHOLOGICAL CHARACTERISTICS, AND ADJUSTMENT IN PARENTS OF CHILDREN WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.
Cappe E, Bolduc M, Rouge MC, et al.
PURPOSE: This study investigated quality of life and adjustment mechanisms in parents of children with Attention-Deficit/Hyperactivity Disorder (ADHD).
METHOD: Ninety parents of children with ADHD completed a sociodemographic questionnaire and self-assessment scales to measure their perceived stress, social support, sense of control, coping strategies and quality of life.
RESULTS: ADHD in children negatively affected parents' quality of life, especially their psychological well-being and personal fulfillment. Family and couple relationships, as well as daily life activities, were also affected. The severity of the disorder, perceiving the situation as a threat or a loss, feeling guilty and holding on to irrational beliefs were related to emotion-focused coping strategies and to a poorer quality of life. Furthermore, hyperactivity index and stress ratings relative to perceiving the situation as a threat or a loss, and adopting emotion-focused coping strategies, predicted poorer quality of life. In contrast, perceiving the situation as challenging was related to a greater sense of control and personal fulfillment. Moreover, perceiving the situation as challenging and adopting problem-focused coping strategies predicted better quality of life.
CONCLUSION: The findings highlight the negative effects of ADHD on parent psychological adjustment and underline the need to recommend training programs that improve parenting skills, parents' perceptions concerning their child's behavior disorder and parental functioning

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Res Dev Disabil. 2018.
ADHD, CD, AND ODD: SYSTEMATIC REVIEW OF GENETIC AND ENVIRONMENTAL RISK FACTORS.
Azeredo A, Moreira D, Barbosa F.
This review aims to analyze the relationships between Attention-Deficit Hyperactivity Disorder (ADHD), Oppositional Defiant Disorder (ODD), and Conduct Disorder (CD), particularly regarding the relative importance of genetic and environmental factors in the development of these disorders. Studies that examined at least two of these disorders were obtained from multiple databases, following the procedures of the Cochrane Collaboration initiative. Of the 279 documents obtained, nine were retained for in-depth analysis and were considered eligible for inclusion. In addition, eight studies from the manual search were included. The objectives, methodological aspects (sample and instruments), and the main conclusions were extracted from each study. Overall, the results suggest that (a) the causes for the onset and maintenance of these disorders are more associated with genetic factors than environmental factors, although the importance of the latter is recognized, and (b) children with ADHD have a predisposition to manifest behaviors that are common to ODD and CD, including the antisocial behavior that these children often display

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Research Journal of Pharmacy and Technology. 2017;10:2395-99.

EFFECT OF PSYCHOMOTOR PROGRAM FOR MATERIAL EXPERIENCE ON THE COORDINATION OF CHILDREN WITH ADHD.

Jung JK, Suh YT.

Background/Objectives: The purpose of this study is to analyze the effects of psychomotor program for material experience on the coordination of children with ADHD.

Methods/Statistical analysis: The subjects of this study were divided into two groups: an experimental group of 8 children and a control group of 8 children, who are all enrolled in the D Children's Development Center and the K Children's Development Center in Seoul. The study was conducted for 12 weeks, twice per week, 60 minutes in for one session. Coordination tests were conducted in the before- and after-session, respectively, for both groups. As a coordination test instrument, the KTK, which was designed and standardized by Kiphard and Schilling in 1974, was used. SPSS 22.0 was used to process the data, and two-way ANOVA was conducted to compare the data between groups and times. The hypothesis testing is fixed to significance level of $p<.05$.

Findings: The results of the analysis were as follows: First, rear balancing MQ1 showed a statistically meaningful difference not only in the interaction effect between time and group, but also in the main effect of time and group. Second, single foot jumping MQ2 showed a statistically meaningful difference not only in the interaction effect between time and group, but also in the main effect of time and group. Third, left and right jumping MQ3 showed a statistically meaningful difference not only in the interaction effect between time and group, but also in the main effect of time and group. Fourth, lateral movement MQ4 showed a statistically meaningful difference not only in the interaction effect between time and group, but also in the main effect of time and group. Fifth, KTK MQT showed a statistically meaningful difference not only in the interaction effect between time and group, but also in the main effect of time and group.

Improvements/Applications: The material experience-based psychomotor program needs to be verified by approaching various subjects as well as ADHD children

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Saudi Medical Journal. 2018;39:52-58.

PREVALENCE OF ATTENTION DEFICIT HYPERACTIVITY DISORDER AND COMORBID PSYCHIATRIC AND BEHAVIORAL PROBLEMS AMONG PRIMARY SCHOOL STUDENTS IN WESTERN SAUDI ARABIA.

Alzaben FN, Sehlo MG, Alghamdi WA, et al.

Objectives: To determine the prevalence of attention deficit hyperactivity disorder (ADHD), subtypes of ADHD, and psychiatric, academic, and behavioral comorbidity in public primary school students in Jeddah, Saudi Arabia.

Methods: This is a cross-sectional study. A simple random sample of 6 primary government schools in Jeddah, Saudi Arabia, was identified (3 male, 3 female), and a random sample of classes in each of grades 1-6 were selected. Between July and November 2016, teachers in these classes were asked to complete the Vanderbilt ADHD scale on all students in their classes.

Results: A total of 929 students were screened. The overall prevalence of ADHD was 5% (5.3% in girls, 4.7% in boys). The most prevalent subtype of ADHD was combined type (2.7%), followed by hyperactive type (1.2%), and inattentive type (1.1%). The highest prevalence of ADHD overall was in grade 3 (7.1%) and the lowest prevalence in grade 6 (3.4%). Among students with ADHD, prevalence of comorbid psychiatric, academic, and behavioral problems was widespread (56.5% oppositional defiant disorder/conduct disorder, 54.4% impaired academic performance, 44.4% classroom behavioral problems, 41.3% depression/ anxiety). Comorbid problems were especially prevalent in combined ADHD subtype and in boys.

Conclusions: Attention deficit hyperactivity disorder is common in primary school children in Jeddah, and is associated with widespread psychiatric, academic, and behavioral problems, especially in boys. These findings have implications for the diagnosis and treatment of this serious neurobehavioral disorder

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Scand J Occup Ther. 2017 May;24:178-86.

SELF-RATING OF DAILY TIME MANAGEMENT IN CHILDREN: PSYCHOMETRIC PROPERTIES OF THE TIME-S.

Skold A, Janeslatt GK.

BACKGROUND: Impaired ability to manage time has been shown in several diagnoses common in childhood. Impaired ability involves activities and participation domain (daily time management, DTM) and body function and structure domain (time-processing ability, TPA). DTM needs to be evaluated from an individual's own perspective. To date, there has been a lack of self-rating instruments for children that focus on DTM.

AIM: The aim of this study is to describe psychometric properties of Time-S when used in children aged 10-17 years with a diagnosis of ADHD, Autism, CP or mild ID. Further, to test whether TPA correlates with self-rated DTM.

MATERIAL AND METHODS: Eighty-three children aged 10-17 years participated in the study. Rasch analysis was used to assess psychometric properties. Correlation analysis was performed between Time-S and a measure of TPA.

RESULTS: The 21 items of the Time-S questionnaire fit into a unitary construct measuring self-perceived daily management of an individual's time. A non-significant, small correlation was found between TPA and DTM.

CONCLUSION AND SIGNIFICANCE: The results indicate good psychometric properties for the questionnaire. The questionnaire is potentially useful in intervention planning and evaluation

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Stress. 2017 Mar;20:149-58.

MOTHERS' PARENTING STRESS IS ASSOCIATED WITH SALIVARY CORTISOL PROFILES IN CHILDREN WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER.

Korpa T, Pervanidou P, Angeli E, et al.

The aim of this study was to explore the relation between mothers' parenting stress and the functioning of the hypothalamic-pituitary-adrenal axis (HPAA), as expressed by daily salivary cortisol concentrations, in their children diagnosed with attention deficit hyperactivity disorder (ADHD). Seventy-five children aged 6-11 years diagnosed with ADHD predominant hyperactive-impulsive/combined (ADHD-HI/C, N = 49) and inattentive symptoms (ADHD-I, N = 26) and 45 healthy peers and their mothers participated in the study. Muothers completed measures assessing their children's ADHD status, perceived parenting stress (Parenting Stress Index - Short Form, PSI-SF), mothers' symptoms of psychopathology, social support and socioeconomic status. Children's salivary cortisol samples were collected at six different time points on a single day. Mothers of children with ADHD-HI/C reported higher levels of parenting stress than mothers of children with ADHD-I and controls. All PSI-SF subscales showed significant associations with children's cortisol awakening response (CAR) in both ADHD groups, with the exception of the parental distress subscale in the ADHD-I group. In both ADHD groups, the parent-child dysfunctional interaction subscale, the difficult child subscale and the PSI total score were significantly associated with children's CAR. An interrelation is revealed between mothers' high levels of parenting stress and HPAA functioning in children with ADHD. In this population, CAR has been identified as a sensitive peripheral measure of HPAA functioning in children. Lay summaryThis study showed that in families of children diagnosed with ADHD, there is a complex relation between the mothers' high levels of parenting stress and children's atypical hypothalamic-pituitary-adrenal axis functioning

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Twin Res Hum Genet. 2017;20:581.

A TWIN STUDY OF THE COMMON GENETIC AND ENVIRONMENTAL INFLUENCES BETWEEN MOTOR CONTROL AND ADHD SYMPTOMS.

Ogliari A, Fagnani C, Pezzica E, et al.

Introduction: In the current study, visuo-motor performances, eval-uated through a haptic interface, and scores of ADHD symptoms, tested by questionnaires, have been analyzed in a sample of young twins from

the general population. The study was aimed at (1) measuring genetic and enviromental contributes related to individual variance of visuo-motor performances inaccuracy and ADHD symptoms by way of univariate method, and (2) examining cooccurrence casual source between ADHD symptoms and a particular motor control performance by bivariate approach.
Materials and Methods: A total of 99 complete pairs aged 6-17 years from the Italian Twin Registry underwent a different motor task, while their parents completed a behavioral questionnaires. A haptic interface was used to deliver a force and record the hand trajectory. Every participant completed the same experimental design, which included several different motor tasks. Univariate and bivariate anal-yses with MX were then applied to psychometric and motor behavioral data.
Results: The analysis results disclosed: (1) how enviro-mental factors are of prime importance to the motor tasks under observation, whereas the additional genetic contributes are of prime importance to ADHD symptoms; and (2) how the co-occurance between the choosen visuo-motor task and ADHD symptom scale is small but signifcant, and how that occurance is explained both by genetic and enviromental factors. It also points out that from one side the additional genetic factors, which are responsible for co-occurance between the traits, are widely the same in the two phe-notypes, while the genetic enviromental contributions are almost entirely separated.
Conclusion: Comparing our results to the preceding study, it emerges that both of them have found a weak but signifcant correlation between the examined motor task and ADHD symptoms, and that the link between these two variables is mainly explained by the common genetic component. In addition, our study found a sizeable overlap between genetic additive factors explaining the correlation between the traits considered. Starting from the results here reported, our research suggests that future study could be carried out using larger samples and more specifc tasks in order to examine the co-occurence among the visuo-motor skills having tighter references with ADHD traits

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Vaccine. 2017.
SUDDEN INFANT DEATH SYNDROME, ATTENTION-DEFICIT/HYPERACTIVITY DISORDER AND VACCINES: LONGITUDINAL POPULATION ANALYSES.
Yang YT, Shaw J.
Concerns about a potential link between sudden infant death syndrome (SIDS), attention deficit and hyperactivity disorder (ADHD) and vaccination are unsupported by longitudinal evidence. The analyses employed a multivariate mixed-effects model analyzing data from the National Immunization Survey, School Vaccination Assessment Reports, National Vital Statistics and National Children's Health Survey. We found that state-level childhood vaccine uptake for age appropriate vaccines was neither associated with the decline in the incidence of SIDS nor rise in the prevalence of ADHD. Our findings provide current and evidence-based information to assist providers counseling vaccine-hesitant parents

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Z Psychosom Med Psychother. 2017 Sep;63:251-66.
PSYCHOANALYTIC PSYCHOTHERAPY FOR CHILDREN AND ADOLESCENTS WITH SEVERE EXTERNALISING PSYCHOPATHOLOGY: AN EFFECTIVENESS TRIAL.
Weitkamp K, Daniels JK, Romer G, et al.
OBJECTIVES: This partly waitlist-controlled prospective field study aimed to evaluate the effectiveness of psychoanalytic psychotherapy for children and adolescents with severe externalising symptoms. Externalising symptoms are associated with diagnoses of conduct disorders, hyperkinetic disorders, and disorders of social functioning.
METHODS: Participants were 93 children and adolescents in psychoanalytic therapy with a diagnosed psychiatric disorder with externalising symptomatology (intervention group: n = 65; minimal supportive treatment/waitlist control group: n = 28). Data was collected from parents and patients (>/= 11 years) at beginning/end of treatment, 6- and 12-month follow-up. The effects of long-term psychoanalytical treatment were analysed using a longitudinal design.

RESULTS: At the end of therapy, externalising symptoms were significantly reduced rated by both parents and patients (parent-rated: d = .69, patient-rated: d = .63). This effect was stable at the 1-year follow-up (parent-rated: d = .77, patient-rated: d = .68). About 70% of the patients may be considered as recovered or improved by the end of therapy.
CONCLUSIONS: Psychoanalytic therapy may be successful in alleviating psychiatric disorders with externalising symptoms with effects stable at the 1-year follow-up

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Zh Nevrologii Psihiatrii im S S Korsakova. 2010;110:67-71.
DIAGNOSIS OF ATTENTION-DEFICIT HYPERACTIVITY DISORDER WITH A CONDITIONED REFLEXES APPROACH.
Albertin SV.
A new conditioned reflexes approach for assessment of attention deficit hyperactivity disorder (ADHD) symptoms in children has been used. Successful solving of behavioral task was related with the ability of children to shift their attention on spatially located sensory signals in radial labyrinth with asymmetric schedule of rewards. The innovative method developed gives a good possibility to increase the accuracy of ADHD evaluation in children of different age as well as to reduce the time for their behavioral testing

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ACAMH THE ASSOCIATION FOR CHILD AND ADOLESCENT MENTAL HEALTH

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Complex effects of dyslexia risk factors account for ADHD traits: evidence from two independent samples

Sara Mascheretti,[1] Vittoria Trezzi,[1] Roberto Giorda,[2] Michel Boivin,[3,4,5] Vickie Plourde,[3,4] Frank Vitaro,[3,6] Mara Brendgen,[3,7] Ginette Dionne,[3,4] and Cecilia Marino[1,8]

[1]Child Psychopathology Unit, Scientific Institute, IRCCS Eugenio Medea, Bosisio Parini; [2]Molecular Biology Lab, Scientific Institute, IRCCS Eugenio Medea, Bosisio Parini, Italy; [3]Research Unit on Children's Psychosocial Maladjustment, Montréal, QC; [4]Ecole de Psychologie, Laval University, Québec, QC, Canada; [5]Institute of Genetic, Neurobiological, and Social Foundations of Child Development, Tomsk State University, Tomsk, Russian Federation; [6]Department of Psycho-Education, GRIP, University of Montreal, Montreal, QC; [7]Department of Psychology, Université du Québec à Montréal, Montreal, QC, ; [8]Centre for Addiction and Mental Health, University of Toronto, Toronto, ON, Canada

Background: Developmental dyslexia (DD) and attention deficit/hyperactivity disorder (ADHD) are among the most common neurodevelopmental disorders, whose etiology involves multiple risk factors. DD and ADHD co-occur in the same individuals much more often than would be expected by chance. Several studies have found significant bivariate heritability, and specific genes associated with either DD or ADHD have been investigated for association in the other disorder. Moreover, there are likely to be gene-by-gene and gene-by-environment interaction effects (G × G and G × E, respectively) underlying the comorbidity between DD and ADHD. We investigated the pleiotropic effects of 19 SNPs spanning five DD genes (*DYX1C1*, *DCDC2*, *KIAA0319*, *ROBO1*, and *GRIN2B*) and seven DD environmental factors (smoke, miscarriage, birth weight, breastfeeding, parental age, socioeconomic status, and parental education) for main, either (a) genetic or (b) environmental, (c) G × G, and (d) G × E upon inattention and hyperactivity/impulsivity. We then attempted replication of these findings in an independent twin cohort. **Methods:** Marker-trait association was analyzed by implementing the Quantitative Transmission Disequilibrium Test (QTDT). Environmental associations were tested by partial correlations. G × G were investigated by a general linear model equation and a family-based association test. G × E were analyzed through a general test for G × E in sib pair-based association analysis of quantitative traits. **Results:** *DCDC2*-rs793862 was associated with hyperactivity/impulsivity *via* G × G (*KIAA0319*) and G × E (miscarriage). Smoke was significantly correlated with hyperactivity/impulsivity. We replicated the *DCDC2* × *KIAA0319* interaction upon hyperactivity/impulsivity in the twin cohort. **Conclusions:** DD genetic (*DCDC2*) and environmental factors (smoke and miscarriage) underlie ADHD traits supporting a potential pleiotropic effect. **Keywords:** Developmental dyslexia; attention deficit/hyperactivity disorder; association study; gene-by-environment interaction; gene-by-gene interaction; pleiotropy.

Introduction

Developmental dyslexia (DD) and attention deficit/hyperactivity disorder (ADHD) are among the most common neurodevelopmental disorders. DD affects about 5–12% of individuals and it is characterized by impaired reading acquisition, in spite of adequate neurological and sensorial conditions, educational opportunities, and normal intelligence. ADHD is characterized by continuous and age-inappropriate deficiency in sustained attention, and/or hyperactive and impulsive behaviors, and it affects approximately 2–10% of school-aged children (American Psychiatric Association, 2013).

Substantial heritability has been reported for both disorders, with estimates ranging from 0.18 to 0.72 for DD (Plomin & Kovas, 2005) and from 0.71 to 0.90 for ADHD (Greven, Harlaar, Dale, & Plomin, 2011; Greven, Rijsdijk, Asherson, & Plomin, 2012; Thapar, Cooper, Eyre, & Langley, 2013). As it is typical for complex heritable disorders, a polygenic multifactorial model best describes the familial aggregation of both DD (Plomin & Kovas, 2005) and ADHD (Thapar et al., 2013).

It is well established, from observations in both clinical and community samples, that DD and ADHD co-occur in the same individuals much more often than would be expected by chance (Grigorenko, 2012). Indeed, across studies around 25–40% of children with either DD or ADHD also meet criteria for the other disorder (Pennington, 2006), and the comorbidity is more pronounced for inattention than for hyperactivity/impulsivity (Plourde et al., 2015; Rosenberg, Pennington, Willcutt, & Olson, 2012). The underlying causes of this co-occurrence are, however, only partially explained. The multiple-deficit model has been proposed as a framework to understand comorbidity (Pennington, 2006) and data are accumulating now in favor of shared etiological risk factors in ADHD–DD (Kere, 2014; Li, Chang, Zhang, Gao, & Wang, 2014; Peterson & Pennington, 2012; Thapar et al., 2013), and in the normal variation of related abilities (Plomin & Kovas, 2005; Plourde et al., 2015).

Investigating the extent to which observable phenotypic correlations are attributable to shared etiological backgrounds, and addressing the issue of

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pleiotropy, are among the major aims of contemporary genetic research (Pennington, 2006, 2015). Several studies have found significant bivariate heritability of ADHD and DD traits in normative samples, which is more pronounced for inattention (estimates from .39 to .60) than for hyperactivity/impulsivity (estimates from .05 to .35) (Greven et al., 2011, 2012; Paloyelis, Rijsdijk, Wood, Asherson, & Kuntsi, 2010; Plourde et al., 2015, submitted; Willcutt, Pennington, et al., 2010). Molecular genetic studies have mapped specific risk loci for DD and ADHD, and some of these are overlapping between the two disorders, for example 3p, 6p, 12p, 15q, suggesting that these latter regions could be the potential sites of the liability underlying ADHD–DD comorbidity (for recent reviews see Kere, 2014; Li et al., 2014). Moreover, specific genes associated with either DD or ADHD have been investigated for association in the other disorder. DD genes *DYX1C1*, *DCDC2*, and *KIAA0319* have been associated with inattention and hyperactivity/impulsivity in a Canadian sample of families with at least one member affected by either DSM-IV-inattention (DSM-IV-I), or DSM-IV-hyperactivity/impulsivity (DSM-IV-HI), or DSM-IV-combined (Couto et al., 2009; Wigg et al., 2004, 2008). As for the ADHD gene *DRD4*, inconsistent results have been reported in DD families. Although evidence for linkage has been reported in a sample of 100 families having at least two siblings affected with DD (Hsiung, Kaplan, Petryshen, Lu, & Field, 2004), no significant associations were found in two independent samples of families with DD (Hsiung et al., 2004; Marino et al., 2003). Notably, none of these studies controlled for concurrent measures of reading or ADHD-related traits, limiting the straightforwardness of their findings.

Besides the main genetic effect, there are likely to be gene-by-gene and gene-by-environment interaction effects (G × G and G × E, respectively) underlying ADHD–DD comorbidity (Pennington, 2006). Additive genetic effects explains only a small proportion of the heritability underlying complex traits (Plomin, 2013), clearly highlighting a major limitation of the polygenic model (Manolio et al., 2009; Plomin, 2013; Zuk et al., 2014). This is known as "the missing heritability problem" (Maher, 2008). Moreover, genes can contribute not only directly but they are also likely to be modulated by, as well as operate by altering sensitivity to, measured environmental risk or protective factors. Until now, G × E have been documented for several disorders, including DD (Friend, DeFries, & Olson, 2008; Mascheretti et al., 2013; Pennington & Bishop, 2009) and ADHD (Grizenko et al., 2012; Rosenberg, Pennington, Willcutt, & Olson, 2011), and they are likely to prove to be important in a broader range of multifactorial conditions (Rutter, Moffitt, & Caspi, 2006). However, as of yet, similar frameworks for exploring the pleiotropic effect of putative risk factors have never been used. Indeed, even if G × G and G × E have been investigated independently in DD (Friend et al., 2008; Harold et al., 2006; Jacobsen, Kleppe, Johansson, Zayats, & Haavik, 2015; Kremen et al., 2005; Ludwig et al., 2008; Mascheretti, Bureau, Trezzi, Giorda, & Marino, 2015; Mascheretti et al., 2013; McGrath et al., 2007; Powers et al., 2013, 2015) and ADHD (Jacobsen et al., 2015; Rosenberg et al., 2012), to our knowledge, their pleiotropic effects across phenotypes have not been tested.

We therefore hypothesize that DD genes and environmental factors could have pleiotropic effects on ADHD traits, including main, G × G, and G × E effects. For the first time, in this study, we tested the pleiotropic effects of 19 SNPs of five well-replicated DD genes (*DYX1C1*, *DCDC2*, *KIAA0319*, *ROBO1*, and *GRIN2B*), and seven DD environmental factors, that is maternal smoking during pregnancy (smoke), risk of miscarriage (miscarriage), birth weight, breastfeeding, parental age, socioeconomic status (SES), and parental education, on concurrent measurements of ADHD traits in families of DD. As DD and ADHD often co-occur (Grigorenko, 2012), the proper conservative approach to target ADHD traits more sharply is to include a composite score of all reading measures as covariate in all analyses. This ensures that potential pleiotropic effects of DD candidate genes upon ADHD traits are not limited to its phenotypic overlap with reading. We then attempted replication of nominal significant findings in one independent sample, that is the Québec Newborn Twin Study cohort (QNTS; Boivin et al., 2013).

Methods

The protocol was approved by the Scientific Review Board, and by the Bioethics Committee of the Scientific Institute, IRCCS Eugenio Medea.

Sample

This study is based on an ongoing project on the genetic basis of DD (Marino et al., 2003, 2004, 2005, 2007, 2011, 2012; Mascheretti et al., 2014; Mascheretti, Facoetti, et al., 2015). To date, the sample consists of 493 unrelated Italian nuclear families of probands affected by DD according to the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV; American Psychiatric Association, 1994) (mean age = 11.45 ± 3.43, male:female ratio = 2:1), and 311 siblings (mean age = 12.52 ± 3.84; male:female ratio = 1:1), of which 108 were affected by DD. Reading measures were available for all offspring from previous studies (Appendix S1, available online). Blood or mouthwash samples were obtained from all offspring and their biological parents. For the present study, families were contacted by phone and asked to participate in a new phase including an assessment of ADHD traits.

Phenotypes' definition

For each offspring, parents were asked to fill out the Conners' Parent Rating Scales–Revised: Long Version (CPRS-R:L; Conners 1989, Conners, Sitarenios, Parker, & Epstein, 1998; for the Italian version, see Nobile, Alberti, & Zuddas, 2007) which rates childhood behavioral problems in subjects aged 3–17 years old, including ADHD traits (Conners et al., 1998).

The scales are shown to have a good reliability and internal consistency (Nobile et al., 2007) and have been previously used for research purposes in the Italian population (Crippa et al., 2015). The CPRS-R:L consists of 80 items rated on a 4-point Likert scale (from "0 = never or rarely observed" to "3 = very often"), and yields 14 subscales. For the current purpose, two subscales were considered, that is DSM-IV-inattention (DSM-IV-I) and DSM-IV-hyperactivity/impulsivity (DSM-IV-HI). All scores were transformed into age- and gender-adjusted T-scores for analyses. Higher scores (T-score ≥ 65) indicate more problems.

Environmental data collection

Parents filled out an *ad hoc* questionnaire (Mascheretti et al., 2013; Mascheretti, Marino, et al., 2015) investigating the following environmental variables: (a) smoke, (b) miscarriage, (c) birth weight, (d) breastfeeding, (e) parental age, (f) SES, and (g) parental education (for a detailed description, see Appendix S1). A subsample of 193 families (403 offspring) had complete environmental data. Descriptive statistics of the environmental variables and phenotypes of this subsample are outlined in Table S1.

Genotyping

Genotyping data for 19 SNPs spanning *DYX1C1*, *DCDC2*, *KIAA0319*, *ROBO1*, and *GRIN2B* were available from previous studies and are described elsewhere (Marino et al., 2005, 2012; Mascheretti et al., 2014; Mascheretti, Facoetti, et al., 2015; Appendix S1). Genotype error checking was completed in PEDSTATS (Wigginton & Abecasis, 2005) and inconsistent genotypes were not considered for further analyses. Allelic frequencies and Hardy–Weinberg equilibrium were calculated in parents (Table 1) by using PBAT (http://www.biostat.harvard.edu/~clange/default.htm; Lange, DeMeo, Silverman, Weiss, & Laird, 2004). Genotype distributions did not significantly deviate from the Hardy–Weinberg equilibrium (HWE).

Table 1 Allele frequencies and Hardy–Weinberg equilibrium's *p*-values in parents

	Marker	Allele	Allele frequency	HWE
DYX1C1	rs3743205	G	.93	.85
		A	.07	
	rs57809907	G	.90	.97
		T	.10	
	rs189983504	C	.89	.35
		G	.11	
DCDC2	READ1	deletion	.07	.82
	rs793862	A	.28	.07
		G	.72	
KIAA0319	rs4504469	C	.63	.18
		T	.37	
	rs203813	G	.68	.97
		T	.33	
	rs9461045	C	.80	.99
		T	.20	
	rs2143340[a]	A	.84	.99
		G	.17	
ROBO1	rs6803202	T	.51	.72
		C	.49	
	rs9853895	C	.60	.55
		T	.34	
	rs333491	A	.51	.27
		G	.49	
	rs7644521	T	.86	.94
		C	.14	
GRIN2B	rs5796555	–	.72	.25
		A	.27	
	rs1012586	G	.69	.30
		C	.31	
	rs2268119	A	.79	.56
		T	.21	
	rs2216128	T	.77	.87
		C	.23	
	rs11609779	C	.80	.99
		T	.20	
	rs2192973	C	.78	.77
		T	.22	

[a]Marker rs2143340A/G is located on intron 2 of the *TTRAP* gene.

Statistical analysis

Given that CPRS-R:L's subscales correlated with reading tasks (mean $r = .20$; Table S2), a composite score of all reading measures was included as covariate in all analyses. To control for multiple testing, we adjusted the significance level of each type of analysis (i.e. genetic association, environment, G × E, and G × G) by the false discovery rate (FDR) method (Storey, 2002). Indeed, FDR has a solid foothold and an increased power when many tests are performed, especially in the context of genomic data research, and represents an attractive alternative to control false-positive error rates (Glickman, Rao, & Schultz, 2014).

Marker-trait association was investigated by QTDT–version 2.5.1 (Abecasis, Cardon, & Cookson, 2000; Appendix S1).

Correlation between environmental factors and ADHD traits was tested by partial correlations controlling for the reading composite (Table S2). All analyses have been implemented with SPSS version 20.0 (IBM Corp., Armonk, NY, Released 2011).

To explore the combined role of genetic and environmental factors on ADHD traits, we used a general test for G × E interaction in sib pair-based association analysis of quantitative traits (Mascheretti et al., 2013; van der Sluis, Dolan, Neale, & Posthuma, 2008), which is an extension of the Fulker, Cherny, Sham, and Hewitt (1999) maximum likelihood variance components analysis of quantitative traits that incorporates environmental main plus G × E effects, and where the association effect is orthogonally decomposed into between-family and within-family effects (Appendix S1). Standardized residuals obtained from regressing the reading composite on ADHD traits were used (Table S2). All analyses were implemented using the R environment (www.r-project.org). Linear-mixed models were estimated using the 'lme' function.

To assess G × G, we applied a two-step approach (Mascheretti, Bureau, et al., 2015): (a) a general linear model equation, whereby the trait is predicted by the main effect of the number of rare alleles of two genes and by the effect of their interaction, and (b) a family-based association test that takes into account both between-family and within-family genetic orthogonal components (De Lobel, Thijs, Kouznetsova, Staessen, & Van Steen, 2012; Appendix S1). First, all possible pairwise G × G are tested, and then significant G × G pairwises are submitted to family-based analyses to control for stratification bias and to strengthen the reliability of significant findings. Standardized residuals obtained from regressing the reading composite on ADHD traits (Table S2) were used as dependent variables. All analyses were implemented using the R environment (www.r-project.org). Linear-mixed models were estimated using the 'lme' function.

Results

Two hundred and thirty-eight unrelated nuclear families with 468 offspring, all of Italian ancestry, participated in this new study. One-hundred and

fifty siblings (65.2%) met the diagnostic criteria of DD. Consistent with previous data (Pennington, 2006), ADHD traits were reported in 30.5% of subjects with DD according to the CPRS-R:L-DSM-IV-Total (T-score ≥ 65), and inattention was more prevalent than hyperactivity/impulsivity (35.8% and 20.7%, respectively). Table 2 shows the descriptive statistics of phenotypic measures in the total sample.

DSM-IV-I showed significant associations with the common alleles 'G' of both rs3743205 and rs57809907 (*DYX1C1;* $\chi^2 = 5.34$; nominal *p*-value = .02; 98 informative families; genetic effect = 6.21, and $\chi^2 = 6.57$; nominal *p*-value = .01; 129 informative families; genetic effect = 6.12, respectively) and with the rare allele 'A' of rs5796555 (*GRIN2B*; $\chi^2 = 4.05$; nominal *p*-value = .04; 246 informative families; genetic effect = 3.11), which did not survive FDR correction (Table S3). Similarly, DSM-IV-HI showed a significant association with the rare allele 'C' of rs6803202 (*ROBO1*; $\chi^2 = 4.96$; nominal *p*-value = .03; 250 informative families; genetic effect = 2.77), which did not survive FDR correction (Table S3).

DSM-IV-I showed significant associations with smoke and miscarriage (nominal *p*-values = .02 and .01, respectively), while DSM-IV-HI was significantly associated with smoke (nominal *p*-value < .01). After FDR correction, only the correlation between smoke and DSM-IV-HI survived ($r = .19$, *q*-value = .01; Table S4).

Several nominal significant G × E were found upon DSM-IV-I and DSM-IV-HI (Table S5). After FDR correction, only rs793862 (*DCDC2*) with miscarriage upon DSM-IV-HI survived. In particular, allele 'G' interacts with the risk of miscarriage ($\beta = -1.70$, $SE = 0.44$, *q*-value = .05; Table S5) to worsen hyperactivity/impulsivity of 1.70 *SD*. In order to account for the presence of G–E correlations, we investigated the relationship between the between-family component of rs793862 as a 'proxy' variable of the parents' genotype, and miscarriage by the Pearson χ^2 test. No association was found ($\chi^2 = 1.56$, $df = 5$, *p*-value = .91) suggesting that G–E correlations might be considered negligible for this pair of predictors.

Several nominal significant G × G were found upon both DSM-IV-I and DSM-IV-HI, although none survived FDR correction (Table S6).

All nominal *p*-values and FDR-adjusted *q*-values for main, G × E, and G × G analyses are reported in Appendix S2.

Replication of nominal significant findings in the QNTS cohort (Boivin et al., 2013)

QNTS is an ongoing prospective longitudinal follow-up of a birth cohort of twins ($n = 662$) born between 1995 and 1998 in the greater Montreal area, Québec, Canada, whose goal is to document developmental aspects of cognitive, behavioral, and social–emotional traits. Inclusion criteria were the fluent use of French or English by the mother and no major medical complications at birth. Blood or mouthwash samples were obtained from 322 twins and their biological parent. Parental authorized consents were obtained for all the included twin pairs. The QNTS had been previously genotyped for a host of DD genetic (M. Boivin, M. Brendgen, G. Dionne, L. Dubois, D. Pérusse, P. Robaey, R.E. Tremblay, F. Vitaro, unpublished data) and environmental factors (Boivin et al., 2013). For the purpose of this study, we included families of dizygotic twins for which inattention, hyperactivity/impulsivity, and reading measures were available, between ages 6 and 8 years, and with *either* genetic *or* environmental factors overlapping those measured in the Italian sample.

This led to a final sample composed of 193 dizygotic twin pairs with complete data on inattention and hyperactivity/impulsivity, reading, rs793862, rs9461045, birth weight, smoke, parental age, and SES (Table S7). The Social Behavior Questionnaire (SBQ; Tremblay, Desmarais-Gervais, Ganon, & Charlebois, 1987) was used to rate inattention and hyperactivity/impulsivity (SBQ-I and SBQ-HI, respectively). Teachers rated the level of ADHD traits within the past 6 months in

Table 2 Descriptive statistics of the selected CPRS-R:L's scale in total sample

	Total Sample ($n = 468$) Age[a] = 141.21 (±39.81) Sex[b] = 63.7%					Probands ($n = 238$) Age[a] = 131.61 (±31.40) Sex[b] = 70.6%		Siblings ($n = 230$) Age[a] = 151.43 (±45.02) Sex[b] = 56.5%		Affected[c] ($n = 318$) Age[a] = 134.54 (±33.80) Sex[b] = 68.6%		Not-affected ($n = 150$) Age[a] = 154.32 (±46.29) Sex[b] = 54.4%	
	Min	Max	Mean (*SD*)	Skew	Kurtosis	Mean	*SD*	Mean	*SD*	Mean	*SD*	Mean	*SD*
DSM-IV-I	38	98	57.71 (13.93)	0.70	−0.26	61.75	13.79	52.98	12.56	60.92	13.89	50.34	10.91
DSM-IV-HI	37	96	52.85 (12.23)	1.08	0.78	54.63	12.32	50.78	11.82	54.26	12.50	49.60	11.07

DSM-IV-I = CPRS-R:L's DSM-IV-inattention subscale; DSM-IV-HI = CPRS-R:L's DSM-IV-hyperactivity/impulsivity subscale.
All scores were transformed into age- and gender-adjusted T-scores according to Italian population norm.
[a]Age was expressed in months.
[b]Percentage of the male was reported.
[c]The affection status was assigned according to the criteria outlined in the text.

Kindergarten and Grade 1 on a 3-point Likert scale (from "0 = never or not true" to "2 = often or very true"). A mean score between teacher ratings collected at both grades was used for further analysis corrected for reading in Grade 2 (see Plourde et al., 2015 and Appendix S1 for a description of the phenotypic measures). A thorough description of ADHD dimensions, reading measures, and their correlation is available in Appendix S1 and Table S8, respectively.

The finding rs793862 × rs9461045 upon hyperactivity/impulsivity that was found significant in the Italian sample was tested for replication in the twin cohort (Table S6).

Rs793862 × rs9461045 were in HWE in both samples, although rs793862 neared significance for deviation in the Italian sample and conditioned the between- and within-component distributions in offspring (Table S9). To control for stratification bias and insure the reliability of findings, we tested G × G between rs793862 and rs9461045 by the family-based association test. Similar to what we observed in the Italian sample, we found a significant interaction (β = .82, *SE* = 0.32, nominal *p*-value = .01) in the QNTS cohort, which survived FDR correction (*q*-value = .03; Appendix S3). This finding means that each additional transmission of the minor allele in the pairwise produces an additional worsening upon DSM-IV-I and SBQ-HI of 0.45 and 0.82 *SD*, respectively, compared to the main effect.

Discussion

In a genetically informed study of 238 Italian families of DD, we explored the hypothesis that five genes (*DYX1C1*, *DCDC2*, *KIAA0319*, *ROBO1*, and *GRIN2B*) and seven environmental factors (smoke, miscarriage, birth weight, breastfeeding, parental age, SES, and parental education) known to influence DD, could also be associated with ADHD traits across the whole distribution of liability, *via* main, G × G, and G × E effects. After controlling for reading traits, we found significant main and interactive associations upon hyperactivity/impulsivity involving *DCDC2*, *KIAA0319*, smoke, and miscarriage, suggesting that these factors exert pleiotropic effects and that complex effects are at play and might be responsible for ADHD–DD comorbidity. Most importantly, we replicated the G × G effect between *DCDC2* and *KIAA0319* upon hyperactivity/impulsivity in the QNTS cohort. Noteworthy, although we relied upon a conservative statistical corrections for multiple testing to infer significance, further validating by replication in an independent cohort adds strength to our G × G findings, as replication provided the strongest evidence that the results are not due to type I error (e.g. Eicher et al., 2014).

In particular, we found that hyperactivity/impulsivity is affected by smoke, which represents one of the most consistent and well-replicated environmental risk factor for ADHD, although the nature of the association is still under debate (Thapar & Rutter, 2009; Thapar, Rice, et al., 2009). Moreover, hyperactivity/impulsivity is modulated by *DCDC2* in interaction with miscarriage. By providing hints about the time window within which miscarriage-related putative hazards potentially exert their action, that is the prenatal period, these results may shed light on some time-sensitive, neurobiological mechanisms underpinning hyperactivity/impulsivity. The prenatal period is indeed a time frame of great anatomical and functional changes in terms of brain development. To the extent that a role in neuronal migration (Burbridge et al., 2008; Meng et al., 2005; Wang et al., 2011) and in ciliary function (Massinen et al., 2011) has been suggested for *DCDC2*, we might hypothesize that miscarriage sets off a cascade of risk events, possibly via epigenetic mechanisms, which negatively modulate *DCDC2* expression, eventually influencing fetal brain cytoarchitecture and development. Previous studies reported detrimental effects of maternal behaviors correlated with prenatal hazards such as miscarriage, acting as hidden predictors upon ADHD (Thapar et al., 2013). From this perspective, our results are consistent with the diathesis-stress model (Rende & Plomin, 1992), whereby a hostile environment may lead to greater genetic liability, which would remain otherwise undetected in more supportive environments.

Finally, concerning G × G finding, the impairment due to *KIAA0319* and *DCDC2* is mostly driven by synergistic rather than main or additive effects (effect sizes range between 0.45 and 0.82 for G × G, and 0.01–0.06 for main effects). These data fit with the reported independence of interaction and main effects at both the statistical (Moffitt, Caspi, & Rutter, 2005) and the biological levels, and further support the investigation of G × G as a crucial approach to catch hidden heritability (Plomin, 2013).

Conclusion

In summary, our data sustain pleiotropic effects upon ADHD for DD susceptibility factors. The estimated statistical power of our study is around 95% both in the Italian sample and in the QNTS cohort (PBAT Power Calculator, http://www.biostat.harvard.edu/Bfbat/pbat.htm; G*POWER version 3.1.5, http://www.ats.ucla.edu/stat/gpower/). Nevertheless, some limitations need to be addressed. First, univariate association analyses should be considered exploratory, and in the future, may be confirmed by newly developed methods for multivariate association analyses of multiple related traits. Second, the significance of the current association findings should be interpreted cautiously until they can be replicated in ADHD families.

Supporting information

Additional Supporting Information may be found in the online version of this article:

Table S1. Descriptive statistics of the environmental and phenotypic variables.

Table S2. Correlation between the selected CPRS-R:L's subscales and reading tasks in the offspring sample.

Table S3. Marker-trait association *p*-values between the *DYX1C1*, *DCDC2*, *ROBO1*, *KIAA0319*, and *GRIN2B* markers on the selected CPRS-R:L's subscales in the total sample (n = 238).

Table S4. Partial correlation between the selected CPRS-R:L's subscales and environmental factors.

Table S5. Results obtained by applying the general test for G × E interaction in sib pair-based association analysis of quantitative traits for *DYX1C1*, *DCDC2*, *ROBO1*, *KIAA0319*, and *GRIN2B* markers and the environmental variables on the selected CPRS-R:L's subscales in which the $i_{\omega kg}I_{kg}$ or $i_{\omega g}$ term was nominally significant.

Table S6. Significant nominal pairwise G × G effects between the *DYX1C1*, *DCDC2*, *ROBO1*, *KIAA0319*, and *GRIN2B* markers on the selected CPRS-R:L's subscales.

Table S7a. Overlapping genotypings between the Italian and QNTS samples.

Table S7b. Overlapping environmental variables between the Italian and QNTS samples.

Table S8. Correlation between the selected CPRS-R:L's subscales and reading tasks in the families of dizygotic twins of the Québec Newborn Twin Study cohort.

Table S9a. Allele frequencies and Hardy–Weinberg equilibrium's *p*-values of *DCDC2*-rs793862 and *KIAA0319*-rs9461045 in parents of the Italian and the Québec Newborn Twin Study cohorts.

Table S9b. Allele frequencies and Hardy–Weinberg equilibrium's *p*-values of *DCDC2*-rs793862 in offspring of the Italian and the Québec Newborn Twin Study cohorts.

Table S9c. Allele frequencies and Hardy–Weinberg equilibrium's *p*-values of *KIAA0319*-rs9461045 in offspring of the Italian and the Québec Newborn Twin Study cohorts.

Appendix S1. Extended methods section.

Appendix S2. Marker-trait association nominal *p*-values and FDR-corrected *q*-values in the Italian sample.

Appendix S3. Nominal *p*-values and FDR-adjusted *q*-values for G × G effects among the DCDC2 and KIAA0319 markers on ADHD-related traits in the QNTS cohort.

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Correspondence

Cecilia Marino, Centre for Addiction and Mental Health (CAMH), University of Toronto, 1001 Queen St W Toronto, ON M6J 1H4, Canada; Email: cecilia.marino@utoronto.ca

and

Sara Mascheretti, Child Psychopathology Unit, Scientific Institute, IRCCS Eugenio Medea via don Luigi Monza, 2023842 Bosisio Parini (Lecco), Italy; Email: sara.mascheretti@bp.lnf.it

Key points

- DD and ADHD are heritable, complex, neurodevelopmental disorders, which are frequently comorbid.
- Data are now in favor of shared etiological risk factors, which can be either genetic or environmental.
- *DCDC2* is associated with hyperactivity/impulsivity through both G × G (with *KIAA0319*) and G × E (miscarriage) effects.
- Maternal smoke during pregnancy is significantly correlated with hyperactivity/impulsivity.
- DD factors show pleiotropic effects upon ADHD traits.

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The Effect of Experimental Supplementation with the Klamath Algae Extract Klamin on Attention-Deficit/Hyperactivity Disorder

Maurizio Cremonte,[1] Davide Sisti,[2] Ilaria Maraucci,[1] Simona Giribone,[1] Evelin Colombo,[3] Marco Bruno Luigi Rocchi,[2] and Stefano Scoglio[3]

[1]*Neurological and Psychiatric Child Unit, Department of Pediatric, Alessandria Hospital, Alessandria, Italy.*
[2]*Department of Biomolecular Sciences, University of Urbino "Carlo Bo," Urbino, Italy.*
[3]*Nutritherapy Research Center, Urbino, Italy.*

ABSTRACT Attention-deficit/hyperactivity disorder (ADHD) is a chronic neurobiological condition with onset in childhood. The disorder is characterized by inattention, impulsivity, and/or motor hyperactivity, which often affect the development and social integration of affected subjects. Phenylethylamine (PEA), naturally contained in the Klamath Lake microalgae and concentrated in the Klamin® extract, is an endogenous molecule with a general neuromodulatory activity. It functions as an activator for the neurotransmission of dopamine and other catecholamines, and very low concentrations of PEA may be associated with specific psychological disorders such as ADHD. The aim of our study was to evaluate the efficacy of the Klamin extract in treating a group of subjects diagnosed with ADHD. Thirty subjects, aged 6–15, who had been diagnosed with ADHD according to the DSM-IV TR criteria, were enrolled. The supplement was administered to all the subjects, who reported to an ADHD clinic for routine follow-up visits. Observations were made and data collected over a 6-month period. After 6 months of therapy the subjects appeared to show significant improvements based on assessments of their overall functioning, behavioral aspects related to inattention and hyperactivity–impulsivity, attention functions in both the selective and sustained component and executive functions. The study appears to confirm the initial hypothesis that the Klamin extract may positively affect the expression of ADHD symptoms. Additional larger studies on the effects of Klamin on ADHD are needed to further investigate the potential of this extract in ADHD treatment.

KEYWORDS: • *algae extract* • *aphanizomenon* • *attention-deficit hyperactivity disorder (ADHD)* • *phenylethylamine* • *supplementations*

INTRODUCTION

ATTENTION-DEFICIT/HYPERACTIVITY DISORDER (ADHD) is defined as a psychiatric disorder characterized by a developmentally inappropriate, pervasive, and persistent pattern of severe inattention, hyperactivity, and/or impulsivity with onset in childhood. The disorder is associated with substantial impairment in social, academic, and/or occupational functioning. It has the highest prevalence in school age children, but in 60-86% of cases, it tends to persist during adolescence, and in 15% of cases, into adulthood.[1] A 2007 epidemiological study on the prevalence of the disorder in childhood and adolescence, based on a review of 102 international studies, showed a global prevalence of about 6.5% in childhood and 2.7% in adolescence. ADHD is common in boys than girls with a ratio of 2.45:1,[2] and prevalence of the disorder has remained stable over the last years.[3] Diagnosis, exclusively clinical to date, is based on the criteria of the Diagnostic and Statistical Manual of Mental Disorders (APA, 2000–2013[4]) or the ICD-10 (WHO, 1992).[5] A complete diagnosis requires observation of the child and the collection of information from his or her parents, teachers and other role models (using questionnaires and semi-structured interviews) to gather information on the child's behavior and functional impairment in multiple contexts. There are currently no diagnostic instrumental and/or laboratory examinations for the diagnosis of ADHD.

The core symptoms of the disorder are inattention, impulsivity, and hyperactivity. These symptoms appear during childhood, are persistent and pervasive in at least two life contexts, and cause significant interference with the child's functioning or development. In 70–80% of cases there is comorbidity with one or more disorders,[6,7] including oppositional-defiant disorder, conduct disorder, anxiety and depression disorders, specific learning disabilities, obsessive compulsive disorder, tics and Tourette's syndrome, and bipolar disorder. The presence of comorbidity significantly worsens ADHD symptoms and complicates the diagnosis and treatment of the disorder.

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Address correspondence to: Davide Sisti, PhD, Department of Biomolecular Sciences, University of Urbino "Carlo Bo," Piazza Rinascimento 6, 61029 Urbino, Italy, E-mail: davide.sisti@uniurb.it

The interaction between genetic and environmental factors during pre- and postnatal life (particularly in the early years) determines a neurobiological predisposition to develop ADHD.[8] The clinical expression of the disorder is influenced by socioenvironmental factors. The evidence of its genetic origin is supported by studies on identical twins and families with multiple affected subjects in whom several candidate genes have been identified.[6,9–12] The genes encoding beta hydroxylase dopamine are considered candidates, and monoamine oxidase (MAO) A, the receptors for dopamine D2, D4, and D5,[13] genes involved in the serotonin circuit,[14–17] and noradrenergic system.[18–20] The disorder involves the dysregulation of catecholamine metabolism in the brain, as shown by structural and functional neuroimaging, animal studies, and clinical response to drugs with noradrenergic activity.[21,22] However, current research suggests that ADHD cannot be attributed to alterations of a single neurotransmitter system and that the disorder is rather the consequence of the interaction between many dysfunctional neurotransmitter systems.[23]

Psychostimulants, the most commonly used drugs in the treatment of ADHD, act on the monoamine transporters: methylphenidate acts mainly on the modulation of the amount of dopamine and noradrenaline present in the intersynaptic space, resulting in the enhancement of deficient dopaminergic transmission,[24] or limitation of a dopaminergic state of hyperactivity.[25,26] Psychostimulants appear particularly effective in enhancing certain neuropsychological functions such as the inhibition of responses, the working memory and the processes of discrimination of stimuli, resulting in an improvement in the subject's performance on tests designed to assess attention, vigilance, verbal and visual learning, and short-term memory.[27] Atomoxetine, which is a selective inhibitor of norepinephrine reuptake at the presynaptic level with minimal activity on the other monoamine transporters, in addition to improving the cardinal ADHD symptoms, is also recommended in cases of comorbidity of oppositional-defiant and anxiety disorders. Clonidine and guanfacine are other nonstimulant medications that are used for the treatment of the disorder,[28] but they are not registered in Italy for ADHD treatment.

Phenylethylamine (PEA) is an endogenous neurotransmitter synthesized by decarboxylation of phenylalanine amino acid in the dopamine neurons of the nigrostriatal pathway.[29] It is normally stored and metabolized in the brain and in peripheral tissues and functions as an activator for the neurotransmission of dopamine and the other catecholamines through two complementary mechanisms: stimulus of the release of dopamine and catecholamines from the brain intraneuronal reserves and inhibition of the reuptake of dopamine and norepinephrine (noradrenaline) in neurons, thus extending their life and action.[29,30]

PEA can be found in some algae,[31] fungi, and bacteria,[32] a variety of plants,[33] some foods (chocolate), the human brain and that of other mammals.[34] Unlike amphetamines, its alpha-methylated derivative, PEA is easily degraded to phenylacetic acid by MAO.[35] PEA belongs to the so-called trace amines,[36] a group of amines present in the intra- and extracellular space at much lower concentrations compared to the biogenic amines and the neurotransmitters related to them such as epinephrine, norepinephrine, serotonin, dopamine, and histamine.[37] Trace amines bind to a receptor associated with the G-protein, called TAAR (trace amine associated receptor).[38,39] It is believed that the binding of PEA to TAAR 1 results in an alteration of the functioning of the monoamine carrier, which leads to inhibition of the reuptake of dopamine, serotonin, and norepinephrine,[40] and an increase in the concentration of these neurotransmitters in the synaptic cleft. Some authors have observed that the urinary excretion of PEA in ADHD subjects is lower than in controls.[41,42] Moreover, patients who benefit from the use of methylphenidate have shown a significant increase in the level of PEA compared to nonresponders.[42] The phycocyanins, present in the Klamath algae extract, are powerful natural inhibitors of MAO-B, thus enabling PEA to reach the brain and perform its action.[43]

Study objective: To evaluate, through a pilot study, the effectiveness of PEA (beta-PEA) and phycocyanins (which have reversible anti MAO-B activity) contained in the Klamin® extract on a group of subjects diagnosed with ADHD.

MATERIALS AND METHODS

The study enrolled a total of thirty patients who had been reporting for at least 3 months to the ADHD outpatient clinic of the Neurological and Psychiatric Child Unit, Pediatric Department, Alessandria Hospital, Italy. The subjects, 2 girls and 28 boys, aged 6–15 (average of 9 years and 6 months), had been diagnosed with ADHD according to the Diagnostic and Statistical Manual of Mental Disorders (DSM) criteria. All the families and patients with a mental age of over 12 were fully informed of the clinically validated pharmacological and nonpharmacological treatments currently available. All the participants agreed to begin the therapeutic trial by signing an informed consent form. Enrollment took place between April 2013 and April 2014 (Table 1).

Inclusion criteria were as follows: aged 6–17, absence of comorbidity with autism spectrum disorder or major psychotic or depressive disorders, no therapy with anticonvulsant or MAO inhibitor drugs.

Out of the 30 subjects, 23 had been diagnosed with ADHD "combined" subtype, while 7 belonged to the "inattentive" subtype. Eighteen subjects had no associated comorbidity, six subjects had an oppositional defiant disorder, four subjects had a specific learning disorder, and two subjects had simple motor tics. Six subjects were mentally retarded (5 mild, 1 medium severity) and the remaining 24 showed an IQ in the normal range.

At enrollment, 13 subjects had already tried various nonpharmacological treatments (psychoeducational therapy, psychomotor treatment and/or speech therapy, parent training interventions). After diagnosis, the remaining subjects had been referred to local services to start treatment. All subjects were given Klamin for 6 months (in liquid form or in tablets) according to the following dosage (Table 2): Klamin, as indicated in its patent contains[44] concentrations of beta-PEA ranging from 11 to 15 mg/g (average of 13 mg/g);

TABLE 1. CLINICAL CHARACTERISTICS OF THE SAMPLE

No. of subjects	30
Age T0 mean ± SD	9.8 ± 2.86
	N *(%)*
Sex	
Male	28 (93.3)
Female	2 (6.7)
Subtype	
I	7 (23.3)
C	23 (76.7)
Comorbidity	
No	18 (60.0)
Tics	2 (6.7)
SLD	4 (13.3)
ODD	6 (20.0)
Global IQ	
Normal	24 (80.0)
MD light	5 (16.7)
MD mean	1 (3.3)
Change to MTF	
No	26 (86.7)
Yes	4 (13.3)

C, combined; I, inattentive; MD, mental delay; MTF, methylphenidate; ODD, oppositional defiant disorder; SD, standard deviation; SLD, specific learning disorder.

AFA-phycocyanins (selective inhibitors of MAO-B) from 5% to 7% of the dried extract; and mycosporine-like amino-acids from 0.8% to 1% of the dried extract.

Twenty-five subjects completed the trial. Before therapy (T0), the clinical condition (weight, height, general and neurological objectivity), vital signs (pulse, PA, baseline temperature), biochemical parameters (complete blood count with formula, liver and kidney function tests, thyroid hormones), and routine urinalysis were evaluated. Urinary excretions of phenylacetic acid and plasma levels of beta-phenylethylamine (PEA) were not evaluated; however, urine levels of the PEA metabolite had been measured in previous investigations.[41,42]

Each patient was also evaluated using international standardized tests that assess the overall functioning of the subject (Child Global Assessment Scale [C-GAS]), behavioral aspects related to inattention and hyperactivity–impulsivity (SNAP IV, Conners' parent rating scale-R), oppositional-defiant disorders (subscale ODD, SNAP IV), attention functions in both the selective and in sustained component (Bell's Test), executive functions (Tower of London test), freedom of distractibility parameter (LD, Wechsler Intelligence Scale for Children III [WISC III scale]), short-term verbal memory (numbers memory, WISC III scale) and arithmetic reasoning, and mental math skills (arithmetic reasoning, WISC III scale).

TABLE 2. KLAMIN DOSAGE USED DURING STUDY

Body weight (kg)	*Dosage of Klamin® in first month of therapy (mg/day)*	*Dosage of Klamin in second to sixth month of therapy (mg/day)*
<25	125	250
>25	300	600
>40	600	1200

In the first, third, and sixth month of treatment, the clinical condition and vital signs were reassessed and the C-GAS scale was completed. Furthermore, in the sixth month (T1, final visit), patients underwent a second hematological control and all the evaluation scales were administered again.

Statistical analysis

Clinical evaluations and logical reasoning tests repeated at the final visit (T1) were compared with pretreatment baseline values (T0), and psychometric test scores after the Klamin treatment were compared with test results at time T0 (before treatment). As part of an "intention to treat" design, the scores of all subjects were included regardless of whether they had finished the Klamin treatment cycle. Statistical analyses were performed using multivariate techniques to show whether the subjects' scores at T1, taken as a whole, were significantly different from their scores at T0. Hence, the multiple analysis of variance for repeated measures was used to highlight the significance of each single questionnaires; the suitable *post hoc* tests were performed after Bonferroni adjustments. Scatter plots were also used; the abscissa shows the initial value, the ordinate shows the difference between the final and initial value. The effects of Klamin were visualized with linear regression; R Pearson coefficients were also calculated to quantify the strength of the correlation between variables. Linear regression slopes were used to assess whether Klamin's effect is dependent on the initial value or if it has a similar effect on all patients, regardless of initial values. The two-tailed significance level was fixed at 0.05. All calculations were performed with SPSS software version 19.0.

RESULTS

All the biochemical parameters (complete blood count with formula, liver and kidney function tests, thyroid hormones) and urinalysis evaluated at T0 e T1 showed values in the normal range. The values, derived from the questionnaires and from the rating scales, were compared for each of the 25 subjects who completed the study at the beginning (T0) and at the end (T1) of the study period. In particular, the overall functioning of the subjects was assessed using questionnaires of clinical detection, both directly (C-Gas) and through the perception of the severity of symptoms by parents (Conners' parent scale); the clinical aspects of inattention and hyperactivity-impulsivity using SNAP IV; the executive functions through the Tower of London Test; the attention functions using the Bell's Test; short-term verbal memory, arithmetic reasoning, and the parameter of freedom from distractibility using WISC III.

Considering the set of all the measured scores, the predictor variable, that is, differences between T0 and T1, was significant ($P = .011$). Reported below are the average ratings and standard deviations (T0 and T1) of each of the variables considered (Table 3). Considering the single independent variables (the specific scores of the tests used), the results of the following assessments were found to be statistically significant: the test that evaluated the overall functioning of the child (C-Gas), assessments of the behavioral aspects

TABLE 3. RESULTS OF MULTIVARIATE ANALYSIS: INITIAL MEAN VALUES IN T0 COLUMN, FINAL MEAN VALUES IN T1

Repeated measures analysis	*Tests of within-subjects contrasts*		
Tests	*T0*	*T1*	P
C-GAS	65.28	70.68	<.001*
SNAP IV inattention	12.64	16.28	.002*
SNAP IV hyperactivity	11.32	14.36	.005*
SNAP IV tot	24.32	30.64	.002*
SNAP IV Subscale ODD	4.72	4.44	.743
Conners'	1.50	1.64	.188
London Tower	−1.42	−0.4	.002*
Arithmetic (WISC III)	6.96	6.84	.513
Memory (WISC III)	7.36	7.4	.885
Score LD (WISC III)	81.83	80.42	.682
Bell's test Quickness	−1.36	−0.8	<.001*
Bell's test Carefulness	−1.85	−0.9	<.001*

*Statistically significant. Values of significativity in *P* column.

C-GAS, Child Global Assessment Scale; WISC III scale, Wechsler Intelligence Scale for Children III.

related to inattention and hyperactivity–impulsivity (SNAP IV scale for both individual aspects and in the totality of symptoms), assessments of the attention functions, both in the selective and in sustained component (Bell's Test), and assessment of the executive functions (Tower of London).

On the other hand, the following tests did not yield results showing statistically significant differences between T0 and T1: short-term verbal memory tests (numbers memory, WISC-III), arithmetic reasoning and mental math skill tests (arithmetic reasoning, WISC-III), freedom from distractibility factor tests (WISC-III), assessment of the perception of the severity of symptoms by parents (Conners' Parents scale), and assessment of oppositional-defiant aspects (ODD subscale of SNAP IV).

In all the graphs, T0 values (in the abscissa) were plotted versus T1-T0 values for the following variables: C-Gas (Fig. 1A); SNAP IV (Fig. 1B–D); Tower of London test (Fig. 1E); and Bell's test (Fig. 1F, G). C-Gas value T1–T0 variations were dependent on the Klamin treatment; variation was slight (about 8%) and did not significantly (slope of linear regression=0.071) depend on the initial values (Fig. 1A); R Pearson (0.224; $P=.282$) showed nonsignificant values. Interestingly, Klamin systematically modified C-Gas scores, improving all initial values for a mean value of 5.4, irrespective of initial values. Bell's carefulness test showed a similar trend to C-GAS; R Pearson did not have a significant value (R=0.134; $P=.53$), while they showed a systematic higher final values, with a mean differences of 0.56. R Pearson values were all significant ($P<.05$ for Bell carefulness and $P<.01$ for the other variables) for the following variables: inattention, hyperactivity, Total SNAP IV, London tower, and Bell's Quickness and Carefulness; Moreover, the linear regression slopes were always <0, indicating a linear inverse correlation between initial values and T1–T0 values. In other words, the higher the initial value, the higher (in absolute value) the variation, which means that the greatest improvements were obtained with higher initial scores.

Vital signs and blood chemistry parameters remained in the normal range throughout the study.

DISCUSSION

Klamin is a specific extract obtained from the *Aphanizomenon flos aquae* microalgae found in Klamath Lake (Oregon). The extract contains high concentrations of beta-PEA,[44] in addition to AFA Phycocyanins (potent selective inhibitors of MAO-B) and other molecules (AFA-phytochrome and algalMycosporin) that feature a selective MAO-B inhibition activity.[44] PEA acts as a general neuromodulator performing different complementary actions according to the needs of the body, and it is rapidly eliminated in the form of phenylacetic acid when no longer needed. PEA, which acts through the inhibition of the reuptake of the neurotransmitters or by supporting the production and release of the catecholamines, can be replenished orally on an ongoing basis. It is present in small amounts in many foods, but in quantities that are too small to be effective. Moreover, if ingested alone, it is rapidly destroyed by specific enzymes, namely the MAO-B, which are active in the liver and intestine. Phycocyanins have the ability to selectively inhibit the MAOs MAO-B, thus protecting the PEA and allowing it to perform its neurological functions.[43]

Some studies have shown a deficiency of PEA in autistic girls with Rett syndrome,[45] in children with Autism Spectrum Disorders and in subjects with learning disabilities.[42,46] Reduced levels of beta-PEA have also been reported in subjects with ADHD (42). It has also been found that methylphenidate only works if and when it manages to stimulate increased production of endogenous PEA.[42] Therefore, for disorders that are characterized by low PEA levels (*e.g.*, ADHD), the synergy of PEA and MAO-B enzyme inhibitors provided by the Klamin extract appear to be a safe alternative to drugs such as amphetamines or methylphenidate, which have undesirable side effects.[37]

ADHD is a complex disorder, and its treatment is multimodal: treatment approaches that combine psychosocial and drug therapies appear to be the most effective.[47] There are currently two drug therapies (methylphenidate and atomoxetine) available in Italy. However, many families and healthcare professionals are reluctant to turn to drug therapy to treat ADHD. In particular, parents may be concerned about possible side effects associated with ADHD drugs or they may reject this option for cultural reasons. Therefore, the study of therapies that could replace or minimize the use of drugs is of growing interest.

In the present investigation we observed significant improvements in the treatment group after 6 months of continuous treatment with Klamin. Specifically, our results show improvement in overall functioning (C-GAS scale), in behavioral aspects related to inattention and hyperactivity impulsivity (SNAP IV scale), in attention functions both in the selective and in the sustained component (Bell's test), and in executive functions (Tower of London test). On the other hand, there were no significant changes in verbal short-term memory (memory of numbers, WISC-III), in

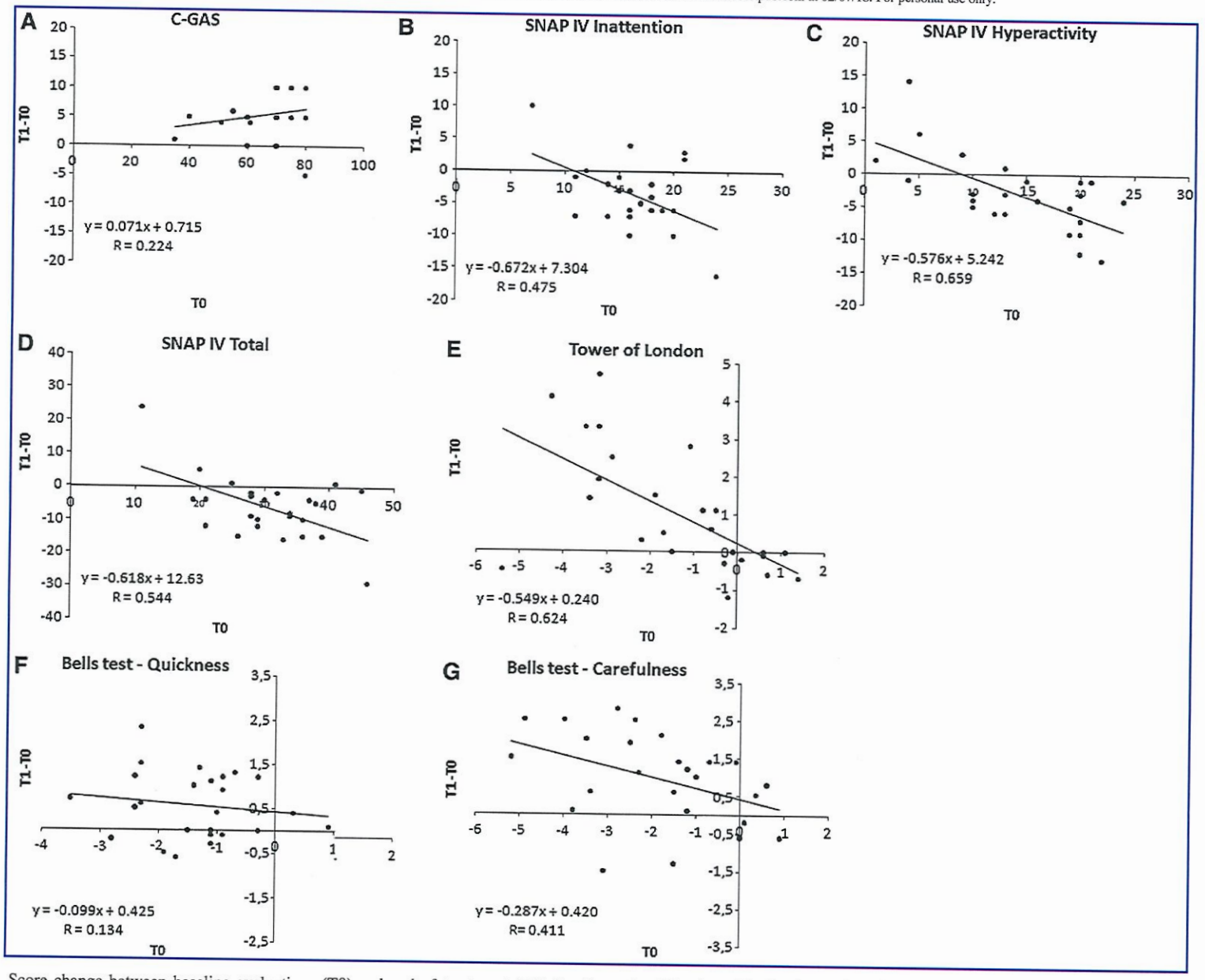

FIG. 1. Score change between baseline evaluations (T0) and end of treatment (T1). In all graphs, T0 values (abscissa) are *plotted* versus T1–T0 values. The following test scores are reported: **(A)** C-GAS; **(B)** SNAP IV Inattention; **(C)** SNAP IV Hyperactivity; **(D)** SNAP IV Total; **(E)** Tower of London; **(F)** Bell's Quickness Test; **(G)** Bell's Carefulness Test. C-GAS, Child Global Assessment Scale; SNAP IV, Rating Scale, revision of the Swanson, Nolan and Pelham Questionnaire.

arithmetic reasoning ability (arithmetic reasoning, WISC-III), in the freedom from distractibility factor of the WISC-III. Moreover, there was no significant change in the perception of the severity of symptoms by parents (Conners parent scale) nor in oppositional-defiant aspects (ODD subscale of SNAP IV).

In conclusion, the study seems to confirm the initial hypothesis that the algal extract Klamin may have a positive impact on the symptoms of ADHD. In particular, our investigation showed statistically significant improvements across all ages in the treatment group in executive and attention functions. Moreover, the severity of symptoms, assessed through a semi-structured interview with the parents, appears to have been reduced.

On the other hand, we found no significant improvements in verbal memory or arithmetic reasoning. Likewise, there were no significant changes in the perception of parents regarding their children's behavior assessed through the Conners' questionnaire, although the severity of symptoms, assessed through a semi-structured interview with parents (inattention-hyperactivity-impulsivity), appeared to be generally reduced for all age groups. Moreover, the C-GAS scale of the child's overall functioning showed significant improvement, especially in patients who continued treatment after the end of study. This difference could be attributed to the parents' high expectations regarding the resolution of their children's behavioral problems. None of the subjects were found to have abnormalities in their vital signs or blood chemistry parameters. Since the subjects are in a developmental phase, it was decided to use BMI instead of body weight to assess possible effects on height-weight growth, and the treatment was found to have no significant impact on the growth of the subjects.

At the end of the study more than 50% of the subjects (13 families) chose to continue the treatment with Klamin, although the product was no longer being provided free of charge and had to be purchased, further confirmation of the apparent tangible and lasting benefits of the treatment. The relatively small sample size did not allow us to analyze possible correlations between age, sex, cognitive level, subtype, and comorbidities. However, these positive preliminary results, especially in light of the fact that the dosages of the Klamin extract used in the study were lower than normal indications, justify further investigations with larger sample sizes (possibly a randomized, controlled, double-blind, multicenter trial).

This is the first study to investigate the overall effects of Klamin on patients formally diagnosed with ADHD, and further investigations are necessary to gain a better understanding of this extract and how its beneficial effects might be heightened.

ETHICS STATEMENT

The study protocol was approved by the Ethics Committee of Alessandria Hospital, Italy—No ASO.Npi.12.01 CE 12/12/2012; authorization and executive determination n. 13 on February 22, 2013 adopted by S.C. G.A.A.S. The study was conducted in accordance with the Declaration of Helsinki and Good Clinical Practice (DM on July 15, 1997).

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AUTHOR DISCLOSURE STATEMENT

S.S. is the R&D Director of the company that owns Klamin's patent, and he is the main inventor of the patent. E.C. is an employee at the same company.

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A TWIN STUDY OF THE COMMON GENETIC AND ENVIRONMENTAL INFLUENCES BETWEEN MOTOR CONTROL AND ADHD SYMPTOMS

Anna Ogliari[2], Corrado Fagnani[1], Elettra Pezzica[2], Raffaella Belotti[2], Emanuele Medda[1], Gabriel Baud-Bovy[2], Marco Battaglia[2], and Maria Antonietta Stazi[1]

[1] *ISS, Rome, Italy*

[2] *Child & Youth Psychiatry, Centre for Addiction and Mental Health, Toronto, Canada*

Introduction: In the current study, visuo-motor performances, evaluated through a haptic interface, and scores of ADHD symptoms, tested by questionnaires, have been analyzed in a sample of young twins from the general population. The study was aimed at (1) measuring genetic and enviromental contributes related to individual variance of visuo-motor performances inaccuracy and ADHD symptoms by way of univariate method, and (2) examining co-occurrence casual source between ADHD symptoms and a particular motor control performance by bivariate approach. *Materials and Methods:* A total of 99 complete pairs aged 6–17 years from the Italian Twin Registry underwent a different motor task, while their parents completed a behavioral questionnaires. A haptic interface was used to deliver a force and record the hand trajectory. Every participant completed the same experimental design, which included several different motor tasks. Univariate and bivariate analyses with MX were then applied to psychometric and motor behavioral data. *Results:* The analysis results disclosed: (1) how enviromental factors are of prime importance to the motor tasks under observation, whereas the additional genetic contributes are of prime importance to ADHD symptoms; and (2) how the co-occurance between the choosen visuo-motor task and ADHD symptom scale is small but significant, and how that occurance is explained both by genetic and enviromental factors. It also points out that from one side the additional genetic factors, which are responsible for co-occurance between the traits, are widely the same in the two phenotypes, while the genetic enviromental contributions are almost entirely separated. *Conclusion:* Comparing our results to the preceding study, it emerges that both of them have found a weak but significant correlation between the examined motor task and ADHD symptoms, and that the link between these two variables is mainly explained by the common genetic component. In addition, our study found a sizeable overlap between genetic additive factors explaining the correlation between the traits considered. Starting from the results here reported, our research suggests that future study could be carried out using larger samples and more specific tasks in order to examine the co-occurence among the visuo-motor skills having tighter references with ADHD traits.

EDITORIALE

"Se fosse cancro ci sarebbe una protesta, ma è salute mentale"

Maurizio Bonati
Dipartimento di Sanità Pubblica
IRCCS – Istituto di Ricerche Farmacologiche Mario Negri, Milano
maurizio.bonati@marionegri.it

La "lotteria" dell'accesso ai Servizi di salute mentale per l'infanzia…

Questo il titolo di un recente "senza esclusione di colpi" nella rubrica *Views and Reviews* del BMJ[1]. Tra le varie considerazioni di Margaret McCartney, *general practitioner* a Glasgow, "ricordiamoci che: l'accesso ai Servizi di salute mentale per l'infanzia è una lotteria, dove l'attesa di anni è la consuetudine; trovare un posto letto libero per un bambino o adolescente presenta difficoltà enormi e immutabili nel tempo; un terzo dei bambini e degli adolescenti inviati al servizio di salute mentale non ha accesso e deve rivolgersi a strutture private. Se si trattasse di cancro ci sarebbe stata una protesta. Ma trattandosi di salute mentale, ci mettiamo un cerotto". In Italia la situazione è peggiore, eppure la reazione non sembra essere diversa. Tra il 2011 e il 2016, la prevalenza delle prestazioni pubbliche per i disturbi neuropsichici dell'infanzia e dell'adolescenza è aumentata del 40-45%, con una crescita annua media del 7%. Sono aumentate le richieste per disturbi specifici dello sviluppo (quali la dislessia e i disturbi del linguaggio) e le richieste per utenti con disabilità o con disturbi psichiatrici di rilevante gravità e complessità. L'accesso ai Servizi di neuropsichiatria dell'età evolutiva varia tra le Regioni tra il 4% e l'8% della popolazione infantile e adolescenziale, a fronte di un bisogno che è più che doppio. Tuttavia, anche nelle realtà apparentemente più virtuose solo 1 utente su 2 riesce ad accedere ai Servizi, e 1 su 3 riceve gli interventi terapeutici di cui avrebbe necessità. In particolare, il continuo incremento di accessi ai Servizi va spesso a discapito di un'adeguata presa in carico dopo la diagnosi. Le famiglie si trovano così costrette a cercare risposte lontano da casa o nel privato, con carichi emotivi, pratici ed economici rilevanti[2].

La Società Italiana di Neuropsichiatria dell'Infanzia e dell'Adolescenza (SINPIA) ha più volte gridato interpretando sia le critiche degli operatori che le lamentele dei pazienti e delle loro famiglie, ma con voce flebile[3]. Anche il 3° Rapporto supplementare del Gruppo CRC (Convenzione sui diritti dell'infanzia e dell'adolescenza)[4], complementare a quello fornito dal Governo e che sarà trasmesso alle Nazione Unite, dopo aver fotografato lo stato delle politiche dell'infanzia dalla prospettiva del terzo settore, a partire dall'esperienza di coloro che lavorano quotidianamente con i bambini e gli adolescenti, ribadisce che l'Italia deve rafforzare Servizi e programmi di qualità per la salute mentale (box).

La politica cosa fa? Valgono le ragioni della politica locale e non il monitoraggio dell'appropriatezza delle prestazioni.

La politica cosa fa? Non è servito ai ragazzi, alle famiglie, agli operatori dei Servizi e all'organizzazione stessa dei Servizi avere un ministro, prima per la famiglia e la solidarietà sociale e poi sottosegretario alla Salute, che fosse neuropsichiatra[5]. A livello regionale, anche per la neuropsichiatria, i modelli assistenziali sono confacenti alle ragioni della politica locale e non al monitorag-

gio dell'appropriatezza delle prestazioni, della valutazione degli esiti, della soddisfazione degli utenti e degli operatori per il miglioramento delle cure. I modelli si moltiplicano differenziandosi, così come le disuguaglianze intra- e inter-regionali, mentre i bisogni rimangono inevasi, fino a quando saranno i budget a guidare le pianificazioni. Così con il decreto del gennaio 2017 tra i nuovi LEA (livelli essenziali di assistenza) sono riconosciuti anche i disturbi dello spettro dell'autismo[6], affinché il Fondo sanitario nazionale abbia il finanziamento per attuare la legge 134 del 2015[7], che a sua volta avrebbe dovuto attuare le linee di indirizzo del 2012 per il completamento delle linee guida del 2011. I tempi della politica, si potrebbe dire, ma nel frattempo? E dopo? I LEA sono da sempre disattesi in quelle Regioni in perenne disavanzo economico e con rientro discrezionale. Quindi, quali essenzialità sono riconosciute? Quale equità? Ma se i giovani pazienti autistici e le loro famiglie possono avere almeno una speranza, quelli con altri disturbi psichiatrici?

Le speranze certo non mancano, in particolar modo quando rappresentano le ultime prospettive di pazienti disperati non presi in carico e di famiglie abbandonate, come è nel caso della salute mentale. Ma anche le speranze sono un indicatore di disuguaglianza perché non nascono ovunque, ma solo dove il *terroir* lo consente. Lo è per esempio il recente "Piano regionale salute mentale" della Regione Friuli Venezia Giulia che, nonostante un modello organizzativo all'avanguardia e le criticità dell'esperienza basagliana, pone tra gli obiettivi principali l'identificazione precoce, la diagnosi, la cura e l'abilitazione/riabilitazione rivolta ai minori con disturbi neuropsichiatrici[8]. Oltre alla definizione dei percorsi di transizione delle cure dall'età pediatrica a quella adulta e all'adozione di linee guida per le emergenze psichiatriche anche per l'infanzia e l'adolescenza.

Anche le speranze sono un indicatore di disuguaglianza.

Il Gruppo CRC, come già negli anni precedenti, raccomanda:

1. **Al Ministero della Salute e alla Commissione Salute della Conferenza delle Regioni** di garantire, attraverso adeguati investimenti di risorse, la presenza omogenea in tutto il territorio nazionale di un sistema integrato di Servizi di Neuropsichiatria infantile, in termini di professionalità e di strutture, in grado di operare in coerente sinergia con pediatri, pedagogisti clinici e altre figure professionali riconosciute, così da garantire i necessari interventi non farmacologici e/o farmacologici, nonché un approccio il più possibile multidisciplinare ai disturbi neuropsichici dell'infanzia e al suo interno Centri di riferimento per patologie particolarmente rilevanti come DCA, autismo, ADHD e riferendo annualmente l'esito dell'azione alla Commissione parlamentare per l'infanzia e l'adolescenza e alla Commissione Salute della Conferenza delle Regioni; dell'adolescenza, strutturando.
2. **Al Ministero della Salute, alla Commissione Salute della Conferenza delle Regioni, all'Istituto Superiore di Sanità, ai Servizi di Neuropsichiatria** di strutturare un adeguato sistema di monitoraggio della salute mentale dei bambini e degli adolescenti, dello stato dei servizi ad essa dedicati e dei percorsi diagnostici e assistenziali dei disturbi neuropsichici nell'età evolutiva, riferendo annualmente l'esito dell'azione alla Commissione parlamentare per l'infanzia e l'adolescenza e alla Commissione Salute della Conferenza della Regioni.
3. **Al Ministero della Salute, al Ministero dell'Istruzione, dell'Università e della Ricerca, alla Commissione Salute della Conferenza delle Regioni** di pianificare interventi coordinati di promozione della salute mentale, con particolare riguardo alla prima infanzia e specifica attenzione alla sensibilizzazione e formazione dei pediatri di famiglia e degli operatori educativi e scolastici, alla prevenzione dei suicidi, dei DCA e di altri analoghi disturbi ad elevato impatto, riferendo annualmente l'esito dell'azione alla Commissione parlamentare per l'infanzia e l'adolescenza e alla Commissione Salute della Conferenza della Regioni. •

La spesa sanitaria nazionale ammonta a 150 miliardi (9% del PIL, prodotto interno lordo). Il Ministro uscente ha affermato che "servono più soldi per il Servizio Sanitario Nazionale. Basterebbero 2-3 miliardi non 150. A breve termine la spesa andrebbe portata al 7% del PIL". Ma per farne che cosa? "Per rispettare il fabbisogno dell'invecchiamento della popolazione", quindi bambini e adolescenti con disabilità anche complesse e croniche non sono contemplati. In campagna elettorale i Programmi sono straordinari, la salute viene da tutti riconosciuta come un diritto. Alcuni (pochi) vanno oltre indicando come interventi necessari (e promessi): la riqualificazione degli ambienti di cura, l'aggiornamento professionale, la formazione sul campo e il potenziamento del personale. Parole di speranza e non Piani d'azione. Tutto il mondo è paese? Forse. Ma il diritto alla salute è universale, individuale e collettivo e va perseguito e promosso come dichiarato nel 1948 dall'OMS e ribadito dall'art. 32 della Costituzione italiana. Tuttavia nonostante la creazione dell'Autorità garante nazionale per l'infanzia e l'adolescenza (2011) e di 16 garanti regionali, oltre ad alcuni metropolitani, le disattenzioni (disuguaglianze) crescono e cronicizzano e la lettura dei dati (bisogni) è condizionata dalle opportunità dei decisori.

Il diritto alla salute: universale, individuale, collettivo e sancito da OMS e dalla nostra Costituzione.

In un'area in cui le povertà si incrociano (quella della psichiatria[9], quella dei bambini e degli adolescenti [1 milione in Italia, il 10% dei minori, vive in condizioni di povertà assoluta[10]], quella della politica[11]) l'essenzialità del senso e dell'utile di un intervento per la comunità necessita di essere recuperata.

In Italia i casi prevalenti vivi dopo una diagnosi di tumore sono circa 3 milioni[9]. Sono oltre 800.000 i bambini e gli adolescenti con bisogni di cure neuropsichiatriche, solo 400.000 accedono ai Servizi di neuropsichiatria dell'età evolutiva, ma solo 150.000 ricevono gli interventi terapeutici prescritti.

Che succederebbe se accadesse lo stesso nei Servizi oncologici? **R&P**

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IRCCS ISTITUTO DI RICERCHE FARMACOLOGICHE MARIO NEGRI
DIPARTIMENTO DI SALUTE PUBBLICA
Laboratorio per la Salute Materno Infantile
Via Giuseppe La Masa, 19 - 20156 Milano MI - Italia - www.marionegri.it tel
+39 02 39014.511 - fax +39 02 3550924 - mother_child@marionegri.i