NEWSLETTER

INDICE:

ISTITUTO DI RICERCHE FARMACOLOGICHE MARIO NEGRI IRCCS

BIBLIOGRAFIA ADHD GENNAIO 2017

Acad Pediatr. 2015 Jul;15:439-43.

EXAMINING TRENDS AND COEXISTING CONDITIONS AMONG CHILDREN QUALIFYING FOR SSI UNDER ADHD, ASD, AND ID.

Pulcini CD, Perrin JM, Houtrow AJ, et al.

OBJECTIVE: To examine the prevalence trends and coexisting conditions in attention-deficit/hyperactivity disorder (ADHD), autism spectrum disorder (ASD), and intellectual disability (ID) in the pediatric Supplemental Security Income (SSI) population and general population.

METHODS: The Social Security Administration (SSA) provided data on primary and secondary diagnoses of children qualifying for SSI for years 2000 to 2011. We compared SSA data with 2000-2011 National Health Interview Survey data on the prevalence of mental health diagnoses among children in the general population living between 0 and 199% of the federal poverty line. We utilized linear regression analysis to test the statistical significance of differences in the trends of the conditions' prevalence.

RESULTS: Over this time period, the SSI population experienced increases in ADHD (5.8%) and ASD (7.2%) and a decrease in ID (-10.3%). Comparison with change in the general population indicated no significant difference in ADHD but significant differences in ASD and ID. Relative percentage changes reflect similar changes. The SSI population qualifying for SSI with ADHD (70.8%) had higher rates of coexisting conditions than the general population (66.1%), but lower rates of coexisting conditions for ASD and ID.

CONCLUSIONS: ADHD is on the rise among children receiving SSI and in the general population. This suggests that the rise of ADHD in the SSI population is expected and does not represent a misallocation of resources. Changes described among the SSI population in ASD and ID may allude to diagnostic/coding trends and/or true changes in prevalence. Limitations arise from the comparability of the 2 data sets

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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.

Acad Pediatr. 2016.

ADVERSE CHILDHOOD EXPERIENCES AND ADHD DIAGNOSIS AT AGE 9 YEARS IN A NATIONAL URBAN SAMPLE.

Jimenez ME, Wade R, Schwartz-Soicher O, et al.

Objective: To examine associations between adverse childhood experiences (ACEs) and attention-deficit/hyperactivity disorder (ADHD) at age 9 years using longitudinal data and assess the extent to which ACEs during middle childhood are independently associated with ADHD at age 9 years.

Methods: We conducted a secondary analysis of data from the Fragile Families urban birth cohort 5- and 9-year interviews. The sample was limited to children for whom mothers were the primary caregiver and mother-reported information on 8 ACEs and ADHD were available at age 5 and 9 years. We examined associations between ACEs and parent-reported ADHD at age 9 years using logistic regression and controlling for potential confounders.

Results: We included 1572 children; 48% were African American, 11% had parent-reported ADHD at age 9 years, 41% and 42% experienced ГёÑ1 ACE by age 5 years and between the ages of 5 and 9 years, respectively. ACEs before age 5 years were associated with ADHD at age 9 years. One, 2, and ГёÑ3 ACEs between age 5 and 9 years were associated with ADHD at age 9 years even after controlling for ACEs before age 5 years and ADHD at age 5 years (adjusted odds ratio [AOR], 1.9; 95% confidence interval [CI], 1.2-3; AOR, 2.1; 95% CI, 1.2-3.8; and AOR, 2.2; 95% CI, 1.1-4.3).

Conclusions: In this study of urban children, ACEs occurring before age 5 years as well as between the ages of 5 and 9 years were associated with ADHD at age 9 years. Even after controlling for early childhood ACEs and ADHD at age 5 years, the association between ADHD and ACEs in middle childhood remained significant, highlighting the importance of screening and intervention throughout childhood

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Acta Med Iran. 2016;54:718-23.

ATTENTION DEFICIT HYPERACTIVITY DISORDER AND ANXIETY IN CHILDREN WITH MALIGNANCY.

Yousefi Chaijan P, Sharafkhah M, Abdolrazaghnejad A, et al.

Attention deficit hyperactivity disorder (ADHD) and Anxiety is the most common childhood psychiatric disorder. Based on studies, these disorders are more prevalent in some chronic disease. This study aimed at investigating the prevalence of ADHD and anxiety in children with malignancy and anxiety in their parents and comparing the results with those of the control group. One hundred, 3-15-year-old children with malignancy and 100 healthy children without malignancy or any chronic disease were included in this casecontrol study as case and control groups, respectively. Subjects were selected from children who were referred to the pediatric ward of Amir Kabir Hospital of Arak, Iran, in the form of simple probability and based on inclusion and exclusion criteria. ADHD and Anxiety were diagnosed by Conner's Parent Rating Scale-48 (CPRS-48) and Hamilton Anxiety Rating Scale (HARS) and were confirmed by psychologist consult. Data were analyzed by Student t-test in SPSS18. ADHD was observed in 23 cases (23%) with malignancy and 5 controls (5%) (P=0.001). In the case group, 57 children (57%) and 45 of their parents (45%) were suffering from anxiety while in the control group the figure was observed in 12 children (12%) and 11 of their parents (11%) (P=0.001). ADHD and anxiety are more common in children with malignancy as compared with children without malignancy and anxiety is also more common in their parents. Therefore, implementing interventions and psychiatric counseling are recommended for these children and their parents

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ADHD Atten Deficit Hyperact Disord. 2017;1-12.

ATOMOXETINE TREATMENT FOR CHILDREN AND ADOLESCENTS WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER (ADHD): A COMPREHENSIVE META-ANALYSIS OF OUTCOMES ON PARENT-RATED CORE SYMPTOMATOLOGY.

Gayleard JL, Mychailyszyn MP.

Attention-Deficit/Hyperactivity Disorder (ADHD) impacts a significant number of children and adolescents and often leads to deleterious functional impairment. Psychostimulant medication has historically been the first line of pharmacological intervention, though recent years have seen greater attention paid to non-stimulant alternatives. The objective of the present study was to conduct the most comprehensive meta-

analysis to date evaluating the efficacy of atomoxetine in reducing core symptomatology of ADHD according to parent report. Selection criteria were applied, and studies were located by searching electronic databases, review of reference sections, and contact with expert researchers; article searching began on 10/01/2013, and the final search was conducted on 09/01/2014. A total of 42 studies met inclusion criteriaΓÇö33 with control groups and 9 withoutΓÇöfor a total sample of 8398 individuals. For those receiving atomoxetine, the summary preΓÇôpost (e.g., standardized mean gain) effect size estimate was 1.37 (95% CI [1.24, 1.51], p < .001); atomoxetine was found to statistically significantly outperform control conditions overall (Z = 4.07, p < .001), though results differed by the type of control group; for instance, when comparing atomoxetine to alternative medications as controls, significant differences were no longer present. The non-stimulant atomoxetine led to significant improvement in core ADHD symptomatology and should be considered as a viable pharmacological treatment option for ADHD

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Am J Med Genet A. 2016 May;170A:1165-73.

OVERLAPPING 16P13.11 DELETION AND GAIN OF COPIES VARIATIONS ASSOCIATED WITH CHILDHOOD ONSET PSYCHOSIS INCLUDE GENES WITH MECHANISTIC IMPLICATIONS FOR AUTISM ASSOCIATED PATHWAYS: TWO CASE REPORTS.

Brownstein CA, Kleiman RJ, Engle EC, et al.

Copy number variability at 16p13.11 has been associated with intellectual disability, autism, schizophrenia, epilepsy, and attention-deficit hyperactivity disorder. Adolescent/adult- onset psychosis has been reported in a subset of these cases. Here, we report on two children with CNVs in 16p13.11 that developed psychosis before the age of 7. The genotype and neuropsychiatric abnormalities of these patients highlight several overlapping genes that have possible mechanistic relevance to pathways previously implicated in Autism Spectrum Disorders, including the mTOR signaling and the ubiquitin-proteasome cascades. A careful screening of the 16p13.11 region is warranted in patients with childhood onset psychosis

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Ann Med -Psychol. 2016.

ADHD AND COMORBID DISORDERS IN PEDOPSYCHIATRY: PSYCHIATRIC PROBLEMS, MEDICAL PROBLEMS, LEARNING DISORDERS AND DEVELOPMENTAL COORDINATION DISORDER.

Masi L, Gignac M.

ADHD is a common disorder for children and is highly comorbid with a number of psychiatric and somatic disorders, which leads to important social consequences. Therefore, it is important to screen for the presence of other disorders when a diagnosis of ADHD is considered. Because of the associated pathologies, the clinical picture of the ADHD is more complex and represents a diagnostic challenge. Furthermore, the prognostic and the future of children with a comorbid ADHD is much more unfavorable than that of children with ADHD only. It is thus necessary to recognize the presentation of ADHD associated with various and frequently comorbid pathologies knowing that those will change according to age and the developmental stage. The objective of this article is to describe these comorbidities. We are going to discuss pathologies most often associated with ADHD and the impact of its symptomatology on psychiatric disorders, medical affections and other disorders such as learning disorder and developmental coordination disorder. Along these lines, we carried out a mini review of ADHD and comorbidities. Results showed that comorbid psychiatric disorders such as conduct disorders, mood disorders and anxiety are among the most frequently associated with ADHD in clinical practice. Disruptive disorders are the most common comorbidities found with ADHD. Among these disorders, oppositional defiant disorder must be distinguished from conduct disorders. Conduct disorders are highly comorbid with ADHD (in more than a third of the cases) and increase the severity of the clinical picture. When children show at the same time ADHD and a conduct disorder, they are at risk to have an antisocial personality disorder as well as addictive disorders in adulthood. Depressive disorders can be triggered by ADHD since these young patients have to face numerous failures and difficulties in their family, social and school lives. With respect to bipolar disorders, links exist with ADHD. Bipolar disorder and ADHD treatment is complex: both thymoregulators and medication of ADHD are

necessary. Finally, anxiety disorders are concomitant in 33 % of ADHD children, an association which deteriorates the symptoms of inattention and distractibility. Furthermore, there is also some overlap between ADHD and addictive behavior, obsessive-compulsive disorder, tics, sleeping disorder and specific learning disorder. There is a high prevalence of the association between ADHD and addictive behaviors in connection with impulsiveness, lack of control, automedication and similarity in the neurobiological circuits. Children with an obsessive-compulsive disorder have ADHD in 33 % of the cases. Although treatments of ADHD and obsessive-compulsive disorder differ, they must be taken simultaneously. It seems that sleeping disorders are not co-occurring with ADHD but intrinsic. Besides, sleeping disorders during childhood can mime an ADHD and complicate the diagnosis to be established, in particular when restless legs syndrome or sleep apnea is present. The comorbidity of ADHD and specific learning disorders is high. Children with specific learning disorders have difficulties staying attentive and their academic performance is often below their full potential, just like the ADHD children. Therefore, clinicians who assess patients for ADHD have to systematically screen for the presence of specific learning disorders and vice versa. Likewise, autistic spectrum disorder and eating disorder are more and more recognized as comorbid entities. The DSM-IV made impossible the concomitance between autism spectrum disorders and ADHD. However, the DSM-5 did recognize the existence of this comorbidity. The association of those two pathologies results in more severe dysfunction for the children, but the treatment of ADHD is going to facilitate the medical care of autism spectrum disorders. ADHD is described as a risk factor for eating disorders. Besides, the co-occurrence of obesity with ADHD is connected to impulsiveness and the tendency to addictive behaviors. Relationships of ADHD with posttraumatic stress disorder and attachment disorder have also been noted. Similarities between ADHD and posttraumatic stress disorder can cause diagnostic errors. Indeed, for both disorders we find the following: agitation, irritability, hypervigilance, sleeping disorders, attention disorders and disorders in the executive functions. Therefore, during the assessment of a child with a clinical picture of ADHD, anamnesis must be completed with the search of traumatic events. On the other hand, attachment disorder can also be confused with ADHD. Difficult temperament can disrupt the process of attachment and is associated with a bigger risk of ADHD. Finally, other medical issues should be considered in the assessment of ADHD: brain injury, epilepsy and obesity for example. ADHD children with a co-occurring condition may be severely impaired and treatment is more complex. ADHD is strongly comorbid with a large number of psychiatric and physical pathologies. It is probably more a set of affections than a homogeneous clinical entity. The longitudinal studies of children with one or several comorbidities showed that the outcome of these children was unfavorable, the association of pathologies causing an important dysfunction. The explanations proposed for this strong tendency of comorbidity with ADHD are that comorbidities have the same risk factors (genetic and environmental) and/or that one of the disorder is a subcategory of another. This leads us to conclude that a better comprehension of the high rates of comorbidities with ADHD is essential to optimize treatment of this condition and prevent some of the negative outcomes associated with comorbid ADHD

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Arthritis and Rheumatology. 2016;68:535-38.

ORAL GLUCOCORTICOIDS AND RATES OF INCIDENT DIABETES MELLITUS AND HYPERTENSION IN CHILDREN WITH JUVENILE IDIOPATHIC ARTHRITIS AND ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.

Horton DB, Xie F, Chen L, et al.

Background/Purpose: Diabetes mellitus (DM) and hypertension (HTN) are well-known toxicities of glucocorticoids (GCs), but the risks of these complications are unclear in children with JIA. We studied rates of new-onset DM and HTN after oral GC exposure compared with non-users separately in children with JIA and children with attentiondeficit/ hyperactivity disorder (ADHD), a non-immune reference population.

Methods: Using Medicaid claims data (2000-2010), we identified children ages 1-18 diagnosed with JIA (based on diagnostic codes ± pharmacy claims) or ADHD (based on diagnostic codes). We studied oral GCs as time-varying exposures based on pharmacy claims after a 9-month GC-free baseline period. Incident DM was defined by new use of insulin or oral antidiabetic drugs; secondary type 2 DM definitions combined diagnoses and pharmacy claims. Incident HTN was defined by new use of antihypertensive drugs combined with diagnoses. We compared absolute rates of new DM and HTN in each cohort and used Cox regression to estimate hazard ratios (HRs) between GC-exposed and - unexposed children.

Results: Children with JIA contributed +2,600 person-years (py) of GC-exposed time and +38,000 py of unexposed time; children with ADHD had +7,500 py exposed to GCs and +1.6 million py unexposed. Compared with non-users, GC users were younger and more likely to be recently hospitalized before study entry. Within disease cohorts, exposed and unexposed groups were similar in terms of sex, race/ethnicity, and prior comorbidities. Compared with the unexposed, incremental rate differences of new DM drug use and type 2 diabetes were 10.4/1,000 py and 4.5/1,000 py in GC users with JIA, respectively, and 5.1/1,000 py and 1.7/1,000 py in GC users with ADHD, respectively (Table). The rate differences for new antihypertensive drug use were of similar magnitude: 15.4/1,000 py greater in GC users with JIA and 4.8/1,000 py greater in GC users with ADHD. After adjusting for age, sex, race/ethnicity, year of study entry, prior comorbidities and medications, and baseline healthcare utilization, GC exposure was associated with new DM drug use in children with JIA: current GC use, aHR 3.4 (95% CI 2.4, 4.8); any prior GC use, aHR 1.7 (95% CI 1.2, 2.4). The associations of GC use with type 2 DM in JIA, and with DM among children with ADHD, were similar (Table). The strength of association between GCs and HTN was even greater: current GC use, aHR 4.5 (95% CI 3.2, 6.2); any prior GC use, aHR 2.4 (95% CI 1.6, 3.6). Results for children with ADHD were also similar (Table).
Conclusion: In children with JIA, current oral glucocorticoid use is associated with a 3-fold increased rate of new treatment for diabetes mellitus and over 4-fold increased rate of new treatment for hypertension. These findings are similar among children with ADHD, but the absolute rates of these complications are higher in children with JIA. More work is needed to clarify how GC dose and duration relate to these toxicities

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Brain Dev. 2016.

NEURAL ALTERATIONS IN ADHD CHILDREN AS INDICATED BY VOXEL-BASED CORTICAL THICKNESS AND MORPHOMETRY ANALYSIS.

Kumar U, Arya A, Agarwal V.

Purpose: Neuroimaging studies provide vital information related to the neurobiology of ADHD, but there still exists a wide gap in relevant information. The present study aimed to elucidate the neuroanatomical alteration in Attention deficit hyperactivity disorder (ADHD) children/adolescents.
Methods: Voxel-based cortical thickness (VBCT) and voxel-based morphometry (VBM) was performed to examine neuroanatomic distinctions in 18 children/adolescents aged 7.5-13. years diagnosed with DSM-IV TR as ADHD (non-medicated). They were compared with 18 healthy matched controls.
Results: VBCT findings in ADHD children/adolescents revealed reduced cortical thickness in the left superior frontal, left orbito-frontal and left dorsal anterior cingulate cortex. VBM findings confirmed decreased gray matter volume in the left orbito frontal, left middle frontal/dorsolateral prefrontal, left middle temporal and left cerebellum in comparison to control group. A decrease in white matter volume was also observed in the left inferior frontal and left calcarine of ADHD children/adolescents.
Conclusion: Results reflect possible abnormal neuroanatomical development patterns in ADHD children

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Brain Dev. 2016.

SHORT-TERM EFFICACY AND TOLERABILITY OF METHYLPHENIDATE IN CHILDREN WITH TRAUMATIC BRAIN INJURY AND ATTENTION PROBLEMS.

Ekinci O, Direk M+, Gunes S, et al.

Purpose: This study aims to investigate the short-term efficacy and tolerability of immediate-release methylphenidate (IR-MPH) in children with a history of traumatic brain injury (TBI).
Methods: Twenty children with TBI (mean age: 12.7. ±. 3.1. years) who had clinically significant attention deficit and/or hyperactivity-impulsivity symptoms and twenty children with primary Attention Deficit Hyperactivity Disorder (ADHD) (mean age: 12.3. ±. 3.05. years) were included. Study measures, which included the Turgay DSM-IV based ADHD rating Scale (T-DSM-IV-S), Conners' Parent Rating Scale (CPRS), Conners' Teacher Rating Scale (CTRS-R) and Clinical Global Impression-Improvement Scale (CGI-I), were

completed at the baseline for both of the groups. For the TBI group, study measures and an adverse effect scale developed by the authors were completed 8. weeks after IR-MPH treatment (10. mg dose t.i.d).
Results: No significant difference was found regarding the baseline scale scores between the study groups. Among children with TBI, most of the scores on T-DSM-IV-S, CPRS and CTRS-R were found to improve significantly after MPH treatment, (p . <. 0.05). 70% (N = 14) of the sample were much improved at the endpoint. MPH was generally well-tolerated (95% had either no adverse effect or mild adverse effects).
Conclusion: In this preliminary open-label study, IR-MPH was found as a safe and effective treatment option for ADHD symptoms after TBI. However, future controlled studies are needed to confirm our findings

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Brain Dev. 2016.

DISINHIBITION IN CHILDREN WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER: CHANGES IN [OXY-HB] ON NEAR-INFRARED SPECTROSCOPY DURING "ROCK, PAPER, SCISSORS" TASK.

Ishii S, Kaga Y, Tando T, et al.

Objective: Attention-deficit/hyperactivity disorder (AD/HD) is a common developmental disorder. Many reports have suggested that symptoms of AD/HD are related to frontal lobe dysfunctions, particularly disinhibition. However, measuring neurological findings with biomarkers during frontal functional tasks has sometimes been difficult in children with AD/HD. This study aimed to investigate frontal inhibitory function objectively in children with AD/HD during "rock, paper, scissors" (RPS) tasks, as a familiar game for Japanese children, using near-infrared spectroscopy (NIRS).
Subjects and methods: Eighteen children with AD/HD were compared with 27 typically developing children (TDC). Children from each group were divided into two age groups: younger, 6-10. years; and older, 11-16. years. Changes in oxygenated hemoglobin [oxy-Hb] were measured in the prefrontal region using NIRS during a 'to lose' RPS task, in which subjects were asked to present the RPS signal that would lose in response to one of the three signals displayed randomly on a computer screen every 2.0. s.
Results: The rate of correct performance with both TDC and AD/HD increased with age. Only in the older group, the rate of correct performance was significantly higher with TDC than with AD/HD. However, children with AD/HD in both age groups showed significantly lower [oxy-Hb] activity in the prefrontal region during the 'to lose' RPS task, particularly in the dorsolateral area.
Conclusions: Our results suggest that prefrontal region activation during the 'to lose' RPS task could offer a biomarker for diagnosing AD/HD, and may help in the early treatment of AD/HD

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Brain Injury. 2016;30:773-74.

IMPACT OF ATTENTION ON HEALTH-RELATED QUALITYOF-LIFE FOLLOWING SEVERE TRAUMATIC BRAIN INJURY IN YOUNG CHILDREN.

Clark B, Breau L, Goez H.

Background: Children experiencing severe traumatic brain injury (TBI) demonstrate long-term impairments. An evaluation of health-related quality-of-life (HRQoL) should be incorporated into standards of care and as an outcome measure in TBI research.
Objectives: (1) Assess HRQoL outcomes after severe TBI using the Multiattribute Health Status Classification System (MHSCS) at 3 and 5 or more years post-injury. (2) Compare the 3 and 5 or more year MHSCS HRQoL outcomes. (3) Consider the role of pre-existing conditions.
Methods: This was a retrospective chart review of 19 children sustaining severe TBI before 12 years. Ethics approval was granted. Variables were analysed using SPSS version 16.0.1. T-tests and Chi-square tests assessed equivalency between groups. Group MHSCS scores were compared using Multivariate Analyses of Variance (Manovas) and Multivariate Analyses of Covariance (Mancovas).
Results: An independent t-test on Total MHSCS scores revealed non-significant differences between groups (t(17) = -1.3, p = 0.20) at 3 and 5 or more years. A MANOVA on MHSCS scale scores showed no significant overall difference in HRQoL between the groups, but univariate tests revealed significant differences for Sensation (F(1,17) = 6.26, p = 0.02), Emotion (F(1.17) = 5.16, p = 0.04) and Cognition (F (1,17) = 5.84, p =

0.03). The 3-year group had more problems with sensation and the 5-year group with Emotion and Cognition. Three Mancova analyses revealed significant multivariate effects on MHSCS scores for pre-existing Emotional Regulation ($F(8,5) = 5.63$, $p = 0.037$) and Social Skills problems ($F(8,4) = 8.71$, $p = 0.026$), but not for ADHD ($F(8,4) = 0.88$, $p = 0.59$).
Conclusions: Our results provide several important pieces of information regarding children's progress after severe TBI. Children sustaining severe TBI early in life experience more difficulties with Cognition and Emotion at 5 or more years than at 3 years in follow-up. There are increasing problems with Emotion and Pain over time relating to emotion regulation and social skills problems presenting shortly after injury. Problems with Sensation are greater at 3 than at 5 or more years follow-up and the presence of ADHD shortly after the initial injury may be a factor in later problems with Emotion, Cognition and Pain. Intervention for ADHD shortly after the initial injury may be a factor in attenuating these later problems

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Brain Injury. 2016;30:741-42.

WHAT CAN THE VIRTUAL CLASSROOM TEACH US ABOUT THE ATTENTION DEFICITS PROFILE OF CHILDREN WITH ABI.

Gilboa Y, Kerrouche B, Longaud A, et al.

Objectives: Attention disorders are usually assessed using standardized neuropsychological assessments. However, everyday failures may be sensitive to impairments that are not evident in a laboratory setting, which might preclude assessment of the full spectrum of real-world dysfunction. The Virtual Classroom (VC) is a virtual reality system that was developed for the assessment of attentional skills in an environment that simulates a real world classroom. The aim of this study was to describe the attention deficits profile of children with ABI in an ecologically valid situation using the VC task and to study discriminant and concurrent validity of the VC in this population, as well as factors influencing performance in the VC.
Methods: Forty-one children with ABI and 35 matched controls, aged 8-16, were assessed using the VC. The reaction patterns of the participants in the VC were recorded and documented using four measures representing four attention components: (1) Sustained attention: total correct hits; (2) Impulsivity: commission errors; (3) Reaction time: measured in ms; and (4) Hyperactivity: measured by head movements tracker. The results of the VC were compared to The Test of Everyday Attention for Children (TEA-Ch), The Conners' Parent Rating Scales-Revised: Short (CPRS-R:S) questionnaire and to demographic and injury severity variables.
Results: In the VC task, the performance of the ABI group was significantly lower than that of the control group for the total correct hits, with 45.2% of children with ABI performing more than 1 SD below the mean of the control group. Significant intercorrelations were found between the VC measures ($r = 0.30$- 0.48, $p < 0.001$). Significant correlations were found between the VC variables and some sub-tests of the TEA-Ch and with the CPRS-R:S. The total correct hits ($r = 0.34$, $p < 0.05$), the commission errors ($r = -.33$, $p < 0.05$) and reaction time ($r = -0.50$, $p < 0.01$) correlated significantly with age (older patients perform better). A significant correlation was found between the commission errors and the cranial radiotherapy dose that the children with malignant brain tumours ($n = 12$) received. The linear regression revealed that, for the entire sample ($n = 74$), the total correct hits of the VC was able to predict 9.7% ($p < 0.008$) of the variance of the ADHD index.
Conclusions: Children with ABI in this study displayed significant impairments in various aspects of attention, with sustained and divided attention being the most impaired. The discriminant and concurrent validity of the VC was relatively good in a sample of children and adolescents with ABI. The attentional performance was found to be related to age, age at injury/diagnosis and treatment (radiotherapy dose). The VC appears to be a sensitive, objective, short, easy to use and ecologically valid assessment tool for use in the diagnosis of attention deficits among children and adolescent with ABI

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Brazilian Journal of Otorhinolaryngology. 2016.

EFFECTS OF DISTRACTORS ON UPRIGHT BALANCE PERFORMANCE IN SCHOOL-AGED CHILDREN WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER, PRELIMINARY STUDY.

Aydinli FE, Çak T, Kirazli MÇ, et al.

INTRODUCTION: Attention deficit hyperactivity disorder is a common impairing neuropsychiatric disorder with onset in early childhood. Almost half of the children with attention deficit hyperactivity disorder also experience a variety of motor-related dysfunctions ranging from fine/gross motor control problems to difficulties in maintaining balance.

OBJECTIVES: The main purpose of this study was to investigate the effects of distractors two different auditory distractors namely, relaxing music and white noise on upright balance performance in children with attention deficit hyperactivity disorder.

METHODS: We compared upright balance performance and the involvement of different sensory systems in the presence of auditory distractors between school-aged children with attention deficit hyperactivity disorder (n=26) and typically developing controls (n=20). Neurocom SMART Balance Master Dynamic Posturography device was used for the sensory organization test. Sensory organization test was repeated three times for each participant in three different test environments.

RESULTS: The balance scores in the silence environment were lower in the attention deficit hyperactivity disorder group but the differences were not statistically significant. In addition to lower balance scores the visual and vestibular ratios were also lower. Auditory distractors affected the general balance performance positively for both groups. More challenging conditions, using an unstable platform with distorted somatosensory signals were more affected. Relaxing music was more effective in the control group, and white noise was more effective in the attention deficit hyperactivity disorder group and the positive effects of white noise became more apparent in challenging conditions.

CONCLUSION: To the best of our knowledge, this is the first study evaluating balance performance in children with attention deficit hyperactivity disorder under the effects of auditory distractors. Although more studies are needed, our results indicate that auditory distractors may have enhancing effects on upright balance performance in children with attention deficit hyperactivity disorder.

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Child Neuropsychol. 2017;23:242-54.

CONTEXT INFLUENCES DECISION-MAKING IN BOYS WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER: A COMPARISON OF TRADITIONAL AND NOVEL CHOICE-IMPULSIVITY PARADIGMS.

Patros CHG, Alderson RM, Lea SE, et al.

Attention-deficit/hyperactivity disorder (ADHD) is characterized by an impaired ability to maintain attention and/or hyperactivity/impulsivity. Impulsivity is frequently defined as the preference for small, immediate rewards over larger, delayed rewards, and has been associated with a variety of negative outcomes such as risky behavior and academic difficulty. Extant studies have uniformly utilized the traditional paradigm of presenting two response choices, which limits the generalization of findings to scenarios in which children/adolescents are faced with dichotomous decisions. The current study is the first to examine the effect of manipulating the number of available response options on impulsive decision-making in boys with and without ADHD. A total of 39 boys (ADHD-á=-á16, typically developing [TD] =-á23) aged 8Γ Çô12-áyears completed a traditional two-choice impulsivity task and a novel five-choice impulsivity task to examine the effect of manipulating the number of choice responses (two vs five) on impulsive decision-making. A five-choice task was utilized as it presents a more continuous array of choice options when compared to the typical two-choice task, and is comparable given its methodological similarity to the two-choice task. Results suggested that boys with ADHD were significantly more impulsive than TD boys during the two-choice task, but not during the five-choice task. Collectively, these findings suggest that ADHD-related impulsivity is not ubiquitous, but rather dependent on variation in demands and/or context. Further, these findings highlight the importance of examining ADHD-related decision-making within the context of alternative paradigms, as the exclusive utilization of two-choice tasks may promote inaccurate conceptualizations of the disorder

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Clin EEG Neurosci. 2015;48:20-32.

QUANTITATIVE EEG IN CHILDREN AND ADULTS WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER.

Markovska-Simoska S, Pop-Jordanova N.

In recent decades, resting state electroencephalographic (EEG) measures have been widely used to document underlying neurophysiological dysfunction in attention deficit hyperactivity disorder (ADHD). Although most EEG studies focus on children, there is a growing interest in adults with ADHD too. The aim of this study was to objectively assess and compare the absolute and relative EEG power as well as the theta/beta ratio in children and adults with ADHD. The evaluated sample comprised 30 male children and 30 male adults with ADHD diagnosed according to DSM-IV criteria. They were compared with 30 boys and 30 male adults matched by age. The mean age (±SD) of the children's group was 9 (±2.44) years and the adult group 35.8 (±8.65) years. EEG was recorded during an eyes-open condition. Spectral analysis of absolute (++V2) and relative power (%) was carried out for 4 frequency bands: delta (2-4 Hz), theta (4-8 Hz), alpha (8-13 Hz), and beta (13-21 Hz). The findings obtained for ADHD children are increased absolute power of slow waves (theta and delta), whereas adults exhibited no differences compared with normal subjects. For the relative power spectra there were no differences between the ADHD and control groups. Across groups, the children showed greater relative power than the adults in the delta and theta bands, but for the higher frequency bands (alpha and beta) the adults showed more relative power than children. Only ADHD children showed greater theta/beta ratio compared to the normal group. Classification analysis showed that ADHD children could be differentiated from the control group by the absolute theta values and theta/beta ratio at Cz, but this was not the case with ADHD adults. The question that should be further explored is if these differences are mainly due to maturation processes or if there is a core difference in cortical arousal between ADHD children and adults

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Clinical Journal of Pain. 2017;33:44-50.

PAIN IS ASSOCIATED WITH POORER GRADES, REDUCED EMOTIONAL WELL-BEING, AND ATTENTION PROBLEMS IN ADOLESCENTS.

Voerman JS, De Klerk C, Heyden KMV, et al.

Objectives: The purpose of the present study was to determine whether pain is associated with specific aspects of academic performance, that is, poorer grades, and with factors critical to an adolescent's academic performance, that is, decreased emotional well-being and attention problems. We hypothesized that the association between pain and school grades is mediated by emotional well-being and attention problems.

Methods: In a cross-sectional study, we collected data from 2215 pupils, ages 12 to 13 years. Pain (no, occasional, and frequent), emotional well-being, and attention problems were measured with self-rating scales. Dutch, English, and math grades were taken as an index of academic performance.

Results: Frequent pain in adolescents was associated with poorer grades (Dutch P=0.02 and math P=0.01). Both occasional and frequent pain were associated with reduced emotional well-being (P<0.001) and reduced self-reported attention (P<0.001). However, the association between pain and lower grades disappeared when controlling for emotional well-being and attention.

Discussion: The present study shows that the association between pain and Dutch adolescents grades is mediated by reduced emotional well-being and attention problems. The association between pain and math grades is mediated by emotional problems. The results suggest that an intervention targeted at pain in adolescents could have a positive effect on their emotional well-being, attention, and school performance

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Clin Pediatr. 2016;55:1358-62.

DEMOGRAPHIC DIFFERENCES AMONG A NATIONAL SAMPLE OF US YOUTH WITH BEHAVIORAL DISORDERS.

Visser SN, Deubler EL, Bitsko RH, et al.

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Clin Psychol Rev. 2017;52:108-23.

META-ANALYSIS OF ORGANIZATIONAL SKILLS INTERVENTIONS FOR CHILDREN AND ADOLESCENTS WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.

Bikic A, Reichow B, McCauley SA, et al.

Background In addition to problems with attention and hyperactivity, children with ADHD present with poor organizational skills required for managing time and materials in academic projects. Organizational skills training (OST) has been increasingly used to address these deficits. We conducted a systematic review and meta-analysis of OST in children with ADHD.

Objectives The objective of this study was to systematically review the evidence of the effects of OST for children with ADHD for organizational skills, attention, and academic performance.

Methods We searched 3 electronic databases to locate randomized controlled trials published in English in peer-reviewed journals comparing OST with parent education, treatment-as-usual, or waitlist control conditions. Standardized mean difference effect sizes from the studies were statistically combined using a random-effects meta-analyses across six outcomes: teacher- and parent-rated organizational skills, teacher- and parent-rated inattention, teacher-rated academic performance, and Grade Point Average (GPA). Risk of bias was assessed for randomization, allocation concealment, blinding of participants and treatment personnel, blinding of outcome assessors, incomplete outcome data, and selective outcome reporting.

Results Twelve studies involving 1054 children (576 treatment, 478 control) were included in the meta-analyses. Weighted mean effect sizes for teacher- and parent-rated outcome measures of organizational skills were g-á=-á0.54 (95% CI 0.17 to 0.91) and g-á=-á0.83 (95% CI 0.32 to 1.34), respectively. Weighted mean effect sizes of teacher- and parent-rated symptoms of inattention were g-á=-á0.26 (95% CI 0.01 to 0.52) and g-á=-á0.56 (95% CI 0.38 to 0.74), respectively. Weighted standardized mean effect size for teacher-rated academic performance and GPA were g-á=-á0.33 (95% CI 0.14 to 0.51) and g-á=-á0.29 (95% CI 0.07 to 0.51), respectively.

Conclusions OST leads to moderate improvements in organizational skills of children with ADHD as rated by teachers and large improvements as rated by parents. More modest improvements were observed on the ratings of symptoms of inattention and academic performance.

Protocol registration PROSPERO (CRD42015019261)

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Comput Intell Neurosci. 2016;2016:8450241.

MEG ANALYSIS OF NEURAL INTERACTIONS IN ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.

Khadmaoui A, Gomez C, Poza J, et al.

The aim of the present study was to explore the interchannel relationships of resting-state brain activity in patients with attention-deficit/hyperactivity disorder (ADHD), one of the most common mental disorders that develop in children. Magnetoencephalographic (MEG) signals were recorded using a 148-channel whole-head magnetometer in 13 patients with ADHD (range: 8-12 years) and 14 control subjects (range: 8-13 years). Three complementary measures (coherence, phase-locking value, and Euclidean distance) were calculated in the conventional MEG frequency bands: delta, theta, alpha, beta, and gamma. Our results showed that the interactions among MEG channels are higher for ADHD patients than for control subjects in all frequency bands. Statistically significant differences were observed for short-distance values within right-anterior and central regions, especially at delta, beta, and gamma-frequency bands ($p < 0.05$; Mann-Whitney U test with false discovery rate correction). These frequency bands also showed statistically significant differences in long-distance interactions, mainly among anterior and central regions, as well as among anterior, central, and other areas. These differences might reflect alterations during brain development in children with ADHD. Our results support the role of frontal abnormalities in ADHD pathophysiology, which may reflect a delay in cortical maturation in the frontal cortex

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Computer Methods and Programs in Biomedicine. 2017;140:241-48.

RELIABILITY AND VALIDITY OF DS-ADHD: A DECISION SUPPORT SYSTEM ON ATTENTION DEFICIT HYPERACTIVITY DISORDERS.

Chu KC, Huang YS, Tseng CF, et al.

Background and objectives The purpose of this study is to examine the reliability of the clinical use of the self-built decision support system, diagnosis-supported attention deficit hyperactivity disorder (DS-ADHD), in an effort to develop the DS-ADHD system, by probing into the development of indicating patterns of past screening support systems for ADHD.

Methods The study collected data based on 107 subjects, who were divided into two groups, non-ADHD and ADHD, based on the doctor's determination, using the DSM-IV diagnostic standards. The two groups then underwent Test of Variables of Attention (TOVA) and DS-ADHD testing. The survey and testing results underwent one-way ANOVA and split-half method statistical analysis, in order to further understand whether there were any differences between the DS-ADHD and the identification tools used in today's clinical trials.

Results The results of the study are as follows: 1) The ROC area between the TOVA and the clinical identification rate is 0.787 (95% confidence interval: 0.701–0.872); 2) The ROC area between the DS-ADHD and the clinical identification rate is 0.867 (95% confidence interval: 0.801–0.933).

Conclusions The study results show that DS-ADHD has the characteristics of screening for ADHD, based on its reliability and validity. It does not display any statistical differences when compared with TOVA systems that are currently on the market. However, the system is more effective and the accuracy rate is better than TOVA. It is a good tool to screen ADHD not only in Chinese children, but also in western country

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Current Problems in Pediatric and Adolescent Health Care. 2016.

PRIMARY PEDIATRIC CARE PSYCHOPHARMACOLOGY: FOCUS ON MEDICATIONS FOR ADHD, DEPRESSION, AND ANXIETY.

Strawn JR, Dobson ET, Giles LL.

The evidence base for psychopharmacologic interventions in youth with depressive and anxiety disorders as well as attention/deficit hyperactivity disorder (ADHD) has dramatically increased over the past two decades. Psychopharmacologic interventions commonly utilized in the pediatric primary care setting-selective serotonin (norepinephrine) reuptake inhibitors (SSRIs/SSNRIs), stimulants and +¦2 agonists-are reviewed. General pharmacologic principles are summarized along with class-related side effects and tolerability concerns (e.g., suicidality and activation in antidepressant-treated youth as well as insomnia, irritability, anorexia in stimulant-treated pediatric patients). Selected landmark trials of antidepressant medications in youth with depressive disorders [Treatment of Adolescent Depression Study (TADS) and the Treatment of SSRI-Resistant Depression Study (TADS)] and anxiety disorders [Child/Adolescent Anxiety Multimodal Study (CAMS) and Child/Adolescent Anxiety Multimodal Extended Long-term Study (CAMELS)] are described in addition to the Multimodal Treatment of ADHD Study. Finally, available data are presented that are related to prediction of treatment outcomes in youth with depressive disorders, anxiety disorders, and ADHD

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Dev Cognitive Neurosci. 2016.

VISUAL SEARCH PERFORMANCE IN INFANTS ASSOCIATES WITH LATER ASD DIAGNOSIS.

Cheung CHM, Bedford R, Johnson MH, et al.

An enhanced ability to detect visual targets amongst distractors, known as visual search (VS), has often been documented in Autism Spectrum Disorders (ASD). Yet, it is unclear when this behaviour emerges in development and if it is specific to ASD. We followed up infants at high and low familial risk for ASD to investigate how early VS abilities links to later ASD diagnosis, the potential underlying mechanisms of this association and the specificity of superior VS to ASD. Clinical diagnosis of ASD as well as dimensional measures of ASD, attention-deficit/hyperactivity disorder (ADHD) and anxiety symptoms were ascertained at 3 years. At 9 and 15 months, but not at age 2 years, high-risk children who later met clinical criteria for

ASD (HR-ASD) had better VS performance than those without later diagnosis and low-risk controls. Although HR-ASD children were also more attentive to the task at 9 months, this did not explain search performance. Superior VS specifically predicted 3 year-old ASD but not ADHD or anxiety symptoms. Our results demonstrate that atypical perception and core ASD symptoms of social interaction and communication are closely and selectively associated during early development, and suggest causal links between perceptual and social features of ASD

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Epilepsia. 2016;57:147.

SHOULD CHILDREN WITH ATTENTION DEFICIT/ HYPERACTIVITY DISORDER (ADHD) AND INTERICTAL EPILEPTIFORM DISCHARGES (IEDS) ON AWAKE EEG BE TREATED WITH ANTIEPILEPTIC DRUGS (AEDS) FOR THEIR ADHD SYMPTOMS?

Socanski D, Herigstad A, Beneventi H, et al.

Purpose: The purpose of this study was to investigate whether treatment with AEDs reduce significantly ADHD symptoms in children with IEDs recorded on baseline routine EEG at the ADHD assessment.

Method: This is a retrospective chart review of 517 children (82.4% male), aged between 6 and 14 years diagnosed with ADHD over a 6 year period (between January 2000 and December 2005). At least one digitized 20 min routine EEG including hyperventilation and photic stimulation during wakefulness without sleep deprivation was conducted in all children at ADHD assessment. IEDs were found in 39 cases, 12 of them had previous epilepsy. The use of AEDs was assessed at baseline, 1 and 2 years follow-up. ADHD symptoms scores were assessed with ADHD IV rating scale, in addition to observation by parents and teachers.

Results: Of the 39 patients with IED, 22 (56.4%) cases were treated with AEDs. 12 of them had previous epilepsy and were already treated with AEDs, 10 were on monotherapy and 2 on polytherapy (because of difficult to treat epilepsy). 27 children had no epilepsy comorbidity. At 1 year follow-up, 22 patients were treated with AEDs (10 without previous epilepsy). At 2 years, 12 cases still used AEDs, 2 of them had no epilepsy and 10 patients with previous epilepsy (8 monotherapy, 2 polytherapy). The use of AEDs was not associated with sufficient reduction of ADHD symptoms. Methylphenidate was introduced to 36/39 (92.3%) of our cases, and initial positive response (assessed after 4-8 weeks of treatment) was found in 30/36 (83.3%).

Conclusion: The use of AEDs alone in treatment of ADHD symptoms in children with IEDs dos not improve ADHD symptoms significantly. ADHD symptoms in ADHD children with IEDs should be treated as other ADHD cases without IEDs

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Eur Child Adolesc Psychiatry. 2017;1-12.

EFFECT OF PARENTAL OBESITY AND GESTATIONAL DIABETES ON CHILD NEUROPSYCHOLOGICAL AND BEHAVIORAL DEVELOPMENT AT 4 YEARS OF AGE: THE RHEA MOTHER-CHILD COHORT, CRETE, GREECE.

Daraki V, Roumeliotaki T, Koutra K, et al.

Studies have suggested an association between maternal obesity pre-pregnancy and gestational diabetes (GDM) with impaired offspring neurodevelopment, but it is not clear if these associations are explained by shared familiar characteristics. We aimed to assess the associations of maternal and paternal obesity, maternal glucose intolerance in early pregnancy and GDM, with offspring neurodevelopment at 4 years of age. We included 772 mother-child pairs from the "Rhea" Mother-Child cohort in Crete, Greece. Data on maternal/paternal body mass index (BMI) and maternal fasting serum samples for glucose and insulin measurements were collected at 12 weeks of gestation. GDM screening was performed at 24-28 weeks. Neurodevelopment at 4 years was assessed using the McCarthy Scales of Children's Abilities. Behavioral difficulties were assessed by Strengths and Difficulties Questionnaire and Attention Deficit Hyperactivity Disorder Test. Multivariate linear regression analyses showed that maternal obesity was associated with a significant score reduction in general cognitive ability (β-coeff -4.03, 95% CI: -7.08, -0.97), perceptual performance (β-coeff -4.60, 95% CI: -7.74, -1.47), quantitative ability (β-coeff -4.43, 95% CI: -7.68, -1.18), and executive functions (β-coeff -4.92, 95% CI: -8.06, -1.78) at 4 years of age, after adjustment for several

confounders and paternal BMI. Maternal obesity was also associated with increased behavioral difficulties (β-coeff 1.22, 95% CI: 0.09, 2.34) and ADHD symptoms (β-coeff 4.28, 95% CI: 1.20, 7.36) at preschool age. Paternal obesity maternal glucose intolerance in early pregnancy and GDM was not associated with child neurodevelopment. These findings suggest that maternal obesity may impair optimal child neurodevelopment at preschool age independently of family shared characteristics

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Eur Child Adolesc Psychiatry. 2017;1-10.

THE ROLE OF SOCIO-ECONOMIC DISADVANTAGE IN THE DEVELOPMENT OF COMORBID EMOTIONAL AND CONDUCT PROBLEMS IN CHILDREN WITH ADHD.

Flouri E, Midouhas E, Ruddy A, et al.

Previous research shows that, compared to children without ADHD, children with ADHD have worse socio-emotional outcomes and more experience of socio-economic disadvantage. In this study, we explored if and how the increased emotional and behavioural difficulties faced by children with ADHD may be accounted for by their more disadvantaged socio-economic circumstances. Our study, using data from 180 children (149 boys) with ADHD from the Millennium Cohort Study, had two aims. First, to examine the role of socio-economic disadvantage in the trajectories of emotional and conduct problems in children with ADHD at ages 3, 5, 7 and 11 years. Second, to explore the roles of the home environment (household chaos) and parenting (quality of emotional support, quality of the parent-child relationship and harsh parental discipline) in mediating any associations between socio-economic disadvantage and child emotional and conduct problems. Using growth curve models, we found that socio-economic disadvantage was associated with emotional and conduct problems but neither the home environment nor parenting attenuated this association. Lower quality of the parent-child relationship and harsher discipline were associated with more conduct problems. It appears that socio-economic disadvantage and parenting contribute independently to the prediction of comorbid psychopathology in children with ADHD

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Eur J Paediatr Neurol. 2016.

SLEEP AND EXECUTIVE FUNCTIONS IN CHILDREN WITH ADHD.

Mao S, Yang R, Gao W, et al.

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Eur J Pediatr. 2016;175:1832.

Can i have your attention? an audit of best practice and patient satisfaction in ADHD assessment and management.

Alabede H, Agarwal M, Cawley P.

Background and aims ADHD is estimated to affect around 1 in 20 of the paediatric population (www.action.org.uk). There are well established NICE guidelines and quality standards to be followed in assessing and managing these children to enable best outcome for them. Aim is to compare management of a cohort of children with ADHD to NICE guidance and standards, and relate findings to previous audit, following introduction of monitoring record sheet. Secondary aim to assess parental /patient satisfaction with treatment.

Methods Retrospective Audit, 42 sets of notes selected from patients reviewed between April and September 2015. Data entered onto proforma, then Excel spreadsheet and analysed.

Results In assessing patients, 100% had screening questionnaires completed to support diagnosis. 87% had a school report. Evidence of meeting DSM IV criteria in 98%. All children assessed for co-existing conditions. 100% of children with severe ADHD treated with methylphenidate as first line treatment. Documentation, monitoring of growth and side effects all above 90% and improved compared to previous audit. 100% parents saw improvement at home, 94% in school. Majority gave satisfaction score of 8 and above (out of 10)

Conclusions We are good at obtaining screening questionnaires, diagnosing based on DSM IV criteria, assessing personal and educational circumstances, family/social circumstances and physical health and for co-existing conditions. We do well on first line drug management and advising parental education programmes as well as monitoring growth and side effects. We need improvement in provision of psychological and behavioural advice 'in house' and transition care of adolescents requires urgent input

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Eur J Pediatr. 2016;175:1618.

THE OUTCOME OF AN ADHD PARENTING GROUP TRAINING PROGRAMME (APEG) IN THE PETERBOROUGH NEURODEVELOPMENTAL SERVICE (NDS).

Ayyash HF, Ogundele M, Wisbey R, et al.

Background and aims There is ample evidence that carefully structured enhanced behavioural parenting programmes are useful in the management of ADHD. We aimed to analyze the outcome of an ADHD group parenting training programme offered by a local district in improving the knowledge and skills of carers.

Methods A pre-/post-training intervention study was carried out for parents of children diagnosed ADHD taking part in a 6-session of evidence-based APEG parenting training programme between 2014 and 2015. The parents rated their confidence on a 6 point scale ranging from 0 (not at all) to 5 (very much). These scores were analysed to compare the parents' precourse and post-course confidence levels about different aspects of ADHD diagnosis and management.

Results A total of 27 parents completed the 53 pre- and post-course questionnaires. The knowledge and understanding of the parents increased significantly about all aspects of ADHD in response to all the 5 questions(Figure 1). There were significantly decreased scoring of 0 to 3 among parents after the course while there was corresponding significantly increased scoring of 4 (little more) and 5 (very much)(Figure 2). The difference between the scores of 0 to 3 and 4 or 5 pre- and postintervention was statistically significant (chi square 239, df 1, p value <0.01).

Conclusions Provision of a psychosocial intervention programme for parents of ADHD children through the APEG course proved to be effective in significantly improving the level of knowledge and understanding of parents regarding several aspects of ADHD diagnosis, symptom identification and behaviour control

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Eur J Pediatr. 2016;175:1417.

HOW DO WE SCREEN FOR ADHD.

Illy K.

There is general concern about the number of children that are diagnosed with ADHD. Diagnosing ADHD is not an easy task. Of course, unlike other medical diagnoses it is not possible to do a blood- or urine test in order to make this diagnosis. There are in fact multiple screening-tests that can be used in order to make the diagnosis more plausible. This lecture is intended to highlight some useful screening-tools. Generally there are screening tools for parents and children and for teachers. There will be special focus on the CBCL (Child Behavior Checklist) and the TRF (Teacher's Report Form). Furthermore it is important to notice that the treatment of ADHD in Children should be custom-made. At the moment Methylphenidate still is one of the most useful treatment-options. We will highlight some of these options

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Eur J Pediatr. 2016;175:1605.

STUDY OF BEHAVIOR AND ATTENTION IN CHILDREN WITH OBSTRUCTIVE SLEEP APNEA AND HYPOPNEA SYNDROME.

Chang L, Mi R.

Background and aims To study the behavior and attention in children with obstructive sleep apnea and hypopnea syndrome

Methods During September 2012 to March 2014, more than five years old 451 children (male 300, female 151) with sleep and breathing problems were consecutively enrolled in this study. Each patient was

monitored by whole night polysomnography(PSG), and the parents completed a Behavior part of Vanderbilt ADHD Parent Rating Scale(VADPRS) and Conners index of hyperactivity(CIH). In VADPRS, when a child had 6 attention defict items with more than 2 scores, he/she was considered as having a tendency of attention defect; when a child had 6 hyperactivity items with more than 2 scores, he/she was considered as having tendency of hyperactivity. Total scores of CIH were more than 15, the child was considered to have a tendency of hyperactivity.
Results 451 children were devided into OSAHS group(n=347) and non- OSAHS(n=104) group according diagnostic criteria of AHI>5. According VADPRS, prevalence of attention defect tendency in OSAHS group was 6.63%, which was significantly higher than in non- OSAHS group (1%,P<0.05); prevalence of hyperactivity was 6.92%, which was higher than in non-OSAHS group, but there was no statistic ally significant difference between two groups(1.92%,P>0.05). According CIH, prevalence of hyperactivity in OSAHS group was 11.24%, which was significantly higher than in non-OSAHS group (1.92%,P<0.05).
Conclusions Children with OSAHS were prone to have attention defect and hyperactivity, even to have ADHD, and parents and doctors should pay more attention to this

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Eur J Pediatr. 2016;175:1819-20.

THE BURDEN OF SCHOOL-AGE CHILDHOOD BEHAVIOURAL DISORDERS AND THEIR CO-MORBIDITIES IN A LOCAL DISTRICT OF NORTH-WEST ENGLAND.

Ogundele M.

Background and aims Referrals of school-age children for assessment of difficult or challenging behavior constitute a major caseload of Neuro-developmental (Community) Paediatricians in the UK. We aimed to evaluate the clinical caseload of a local district Community Paediatric unit of a large NHS Trust in the North West of England.
Methods The record of all school-age children referred for challenging behavioral problems seen between Jan 2014 and Oct 2015 were retrospectively analysed.
Results A total of 143 children were seen within the 22-month study period including 128 new referrals and 15 others for follow up. Themale-female ratio was 2.3:1. This corresponds to a prevalence of 1% of the school-age childhood population of 16432 (Mid 2014 estimate). ADHD assessment with standard questionnaires was unconfirmed in 65 cases (45%). Mean age at referral was 8 years 9 months (SD 35 months). Each patient attended on average 2 outpatient clinics with an average follow-up duration of 6 months. 92% of the patients had on average two other co-morbidities (Table 1), including sleep difficulties (40%), Social Communication concerns (25%), learning difficulties (24%), DCD (dyspraxia) (15%) developmental delay (10%) and emotional problems (8.4%). There was history of family and social adversities including separated parents (24%), fostered / adopted (11%) and previous exposure to abuse, domestic violence or neglect (9%). TABLE 1
Conclusions Behavioural problems is common among school-age population. The high levels of social, emotional, developmental and educational cooccurring difficulties emphasize the need for an integrated multidisciplinary and multi-agency collaboration to ensure the best outcome for the affected children and their families. (Table Presented)

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Eur Neuropsychopharmacol. 2016;26:S744-S745.

ATTENTION DEFICIT HYPERACTIVITY DISORDER RATING SCALE: VALIDATION OF A SPANISH VERSION AND A PROPOSAL OF A SHORT-VERSION SCALE.

Vallejo Valdivielso M, D+¡ez-Su+írez A, De Castro Manglano P, et al.

Introduction: Attention-deficit/hyperactivity disorder (ADHD) is a neurodevelopmental disorder that involves an exhibition of developmentally inappropriate levels of inattention (IA) and/or hyperactivity-impulsivity (HI) [1]. Factor analytic findings of ADHD symptoms according to DSM-IV criteria yield an underlying two-factor structure (IA and HI) [2]. The current study use data from two samples of children with and without ADHD.

The purposes were to describe the presence of ADHD symptoms both in non-ADHD and ADHD participants; and to validate a Spanish version of the 18-item ADHD rating scale IV (ADHD-RS-IV).
Methods: Six hundred and twenty-nine subjects were selected for inclusion in the observational study. Two separate samples were included in this study. 495 drug naïve patients aged 6-18 years with an ADHD diagnosis (of all subtypes) were included in the study. 134 healthy controls aged 6-18 years were also enrolled in the study. Confirmatory Factor Analysis was performed with Stata 12.1. using Structural Equation Modeling (SEM) on a polychoric correlation matrix, and maximum likelihood estimation method. SPSS v.20 program was used to calculate corrected itemtotal correlations, to assess discriminant validity, and to determine a cut-off score for the scale and its predictive performance, using ROC analysis. The short version of the ADHD rating scale was developed using a stepwise logistic regression.
Results: ADHD patients had significantly higher scores in all inattention and hyperactivity/impulsive symptoms ($p<0.001$) than the control participants. The receiver operating characteristics (ROC) curve showed that the ADHD-RS Spanish version score had a sensitivity of 91.9% and a specificity of 90.3%. The internal consistency was high for both the ADHD-R-IV and its subscales. The Cronbach's alpha coefficient was 0.94 for the total scale, and ΓëÑ0.90 for the subscales. Ordinal alpha values were 0.95 for the total scale, and ΓëÑ0.90 for the subscales. Confirmatory factor analysis (CFA) showed best fit for a two-factor model of intercorrelated factors: inattention and hyperactivity. The questionnaire offered good discriminant power between ADHD patients and controls (AUC= 0.97). Based on stepwise logistic regression to optimize concordance with the original ADHD-RS, we developed a 6-item version of the scale which presented high internal consistency (Cronbach's alpha = 0.86; ordinal alpha = 0.90), and discriminatory power (AUC= 0.98).
Conclusions: The Spanish version of ADHD-RS-IV analyzed in this study showed a two-factor internal structure that corresponds to DSM-IV and DSM-5 models, and to the one proposed by the author of the original scale. Furthermore, the Spanish ADHD-RS-IV has high discriminatory power resulting in a valid and reliable instrument to measure ADHD symptoms in Spanish population. The 6-item version (items 3, 4, 6 and 8 of IA; and item 2 and 8 of HA) offers a similar discriminatory power to the one of the 18-item scale, suggesting that the abbreviated scale may be used as a screening tool in the pediatric population

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Eur Neuropsychopharmacol. 2016;26:S727.

AGE-RELATED PHARMACOTHERAPY OF ATTENTION DEFICIT HYPERACTIVITY DISORDER IN SLOVENIA IN CHILDREN AND ADOLESCENTS: A POPULATION-BASED STUDY.

Stuhec M, Vedernjak U, Locatelli I.

Brief Introduction: In most European countries there is no data on age-related pharmacotherapy for Attention Deficit Hyperactivity Disorder (ADHD) medicines in children and adolescents. Stimulants are the first line treatments for ADHD treatment and non-stimulants are the second line treatment in children and adolescents and adults [1,2]. Children and adolescents with serious ADHD symptoms should begin their treatment very early. However, for most drugs the efficacy has not been studied in children under six years old and therefore a pharmacotherapy in these patients should be avoided [2].
Aim: The main aim of this research was to obtain the data on age-related ADHD treatment with pharmacotherapy in Slovenia in children and adolescents from 2003 to 2012.
Methods used: Only immediate-release methylphenidate (IRMPH), methylphenidate-osmotic release oral delivery system (OROS-MPH) and atomoxetine (ATX) have been available in Slovenia and included in this study. A prescription per patient within study period was obtained. Outcomes were divided to the 3 different age categories (2-5 years, 6-12 years and 12-17 years). The national consumption was obtained from database of the Health Insurance Institute of Slovenia. The database offers information on the national consumption and cost of the medicines dispensed in Slovenian outpatient pharmacy. This database does not cover the hospital drug consumption from hospital and selfpaid medicines. Ethical approval for the study was obtained from the National Medical Ethics Committee of the Republic of Slovenia in 2012.
Summary of results: Less than 50% of patients with diagnosed ADHD are treated with medications in Slovenia (44.7% in 2012). 5 patients were treated with ATX and 23 patients with MPH (2-5 years' category) within the study period. In the age category 6-12 years, the total number of treated patients with MPH was almost equal for each year within the study period (549-646 patients). However, in the age category 12-17 years the total number of treated patients with MPH increased from 288 in 2002 to 498 in 2012 (72.9%

increase). In the patients treated with ATX in the age category 6-12 years, the total number of treated patients with ATX increased from 8 in 2006 to 157 in 2011 and decreased to 121 in 2012. In the age category 12-17 years the total number of treated patients with ATX increased from 6 in 2006 to 95 in 2010 and to 147 in 2012 (24.5-fold increase). In 2012 22.8% treated patients were treated with ATX.
Conclusions: In the last decade in Slovenia the total number of treated patients with ADHD increased rapidly in all age categories, which indicates a positive trend, although many patients are still untreated. Prescribing to the patients under six years old exists in Slovenia and should be avoided. Higher percentage of ATX treated ADHD patients can also be connected with possible inappropriate prescribing and low respect to the treatment guidelines

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Eur Neuropsychopharmacol. 2016;26:S195-S196.

GENETIC AND NEUROPSYCHOLOGICAL DETERMINANTS OF INCREASED RISK OF OVERWEIGHT IN ADHD BOYS.

Slopien A, Hanc T, Borkowska A, et al.

Introduction: Attention-deficit/hyperactivity disorder (ADHD) as one of the obesity risk factors has been intensively investigated. Studies in recent years have shown that ADHD is associated with a higher risk of overweight and obesity in school-aged children and adolescents (Han-ç et al., 2015b). In recent years, there have been few attempts to explain the genetic background of comorbidity of these disease units (Albayrak et al., 2013). What is more, the co-occurrence of ADHD and obesity can also be associated with deficits in executive functions. Previous studies indicate that a deficit in executive functions occurs both in obese children and adolescents (Reinert, Po'e & Barkin, 2013) as well as in patients with ADHD (Willcutt et al., 2005), but only few studies have tested deficits in executive functions and self-regulation as a possible cause of increased risk of obesity in children with ADHD, and their results are contradictory. Moreover, because the deficits in the executive functions can be shared by ADHD and obesity phenotype developing on the genetic background, it seems reasonable to carry out studies analyzing the total contribution of candidate genes for ADHD and deficit in executive function as determinants of the risk of obesity in patients with ADHD.
Aim: The aim of the study was to assess the relationship of overweight, among children with ADHD, and the polymorphisms of selected candidate genes and deficits in the executive functions.
Methods: The study group was composed of 109 unrelated boys with a diagnosed ADHD, aged 7-18 years. The study analyzed: DRD2 (polymorphism rs1799732), DRD3 (rs6280), DRD4 (rs1800955, rs1800443, 48 VNTR), DAT (rs27072, rs463379, VNTR 3' UTR), COMT (rs4680), SNAP25 (rs363039, rs363043, rs363050), 5HTR2A (rs17288723), BDNF (rs6265). The following tests were used to evaluate the executive function levels: CPT, SC-WIT, TMT, MFFT, VFT, ROCF, WCST. Statistical analysis was performed using: Pearson's chi squared test, Fisher's test, ANOVA test, the Mann-Whitney U test, k-means clustering analysis, logistic regression.
Results: Overweight was present in 20 boys (18.35%) and obesity in 4 (3.6%). Due to a small number of overweight boys the prevalence of overweight, understood as abnormally elevated body mass, was evaluated in all analyses. Statistically significantly less frequently present in the overweight group of patients were: T allele of rs1800955 DRD4 ($p = 0.03$), A allele of rs363039 SNAP25 ($p = 0.04$), C allele of rs363043 SNAP25 ($p = 0.01$) and C allele of rs17288723 5HTR2A ($p = 0.04$). CT and TT genotypes of polymorphism rs1800955, DRD4 gene ($p = 0.03$) were related to lower prevalence of overweight than CC, similarly to rs363039 SNAP25 GA and AA ($p = 0.04$) in comparison with GG. However, TT genotype of rs363043 SNAP25 was related to significantly increased risk of overweight in relation to TC and CC ($p = 0.02$). The analysis did not show any statistically significant differences in the levels of neuropsychological test results between the patients with and without overweight.
Conclusions: Overweight in ADHD boys is related to a single nucleotide polymorphism of 3 candidate genes: rs1800955 DRD4, rs363039 i rs363043 SNAP25 and rs17288723 5HTR2A but not to deficiency determinants in selected executive functions

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Eur Neuropsychopharmacol. 2016;26:S354.

AGE-RELATED PHARMACOTHERAPY FOR ATTENTION DEFICIT HYPERACTIVITY DISORDER IN SLOVENIAN ADULTS: A POPULATION-BASED STUDY.

Stuhec M, Vedernjak U, Locatelli I.

Introduction: In most European countries there are no data on age-related pharmacotherapy for Attention Deficit Hyperactivity Disorder (ADHD) in adults. The pooled prevalence of adult ADHD is 2.5% in the general population worldwide [1]. Evidence suggests that approximately 50% of children with ADHD may continue to suffer from attention problems into adulthood and therefore the percentage of adults receiving treatment for ADHD would be expected to be higher than it is presently. In adults with ADHD, pharmacotherapy is the first-line treatment [2].

Aim: This study used nationwide population-based data to investigate the rate of pharmacological treatment for adults with ADHD in Slovenia from 2003 to 2012.

Methods used: Only immediate-release methylphenidate (IR-MPH), methylphenidate-osmotic release oral delivery system (OROS-MPH) and atomoxetine (ATX) have been available in Slovenia and these were included in this study. Only ATX was approved for adults with ADHD in Slovenia in 2013. For every patient, the prescription within the study period was obtained. Outcomes were divided into 3 age categories (18-24 years, 25-49 years and >50 years). The national consumption of the medications was obtained from the database of the Health Insurance Institute of Slovenia. The database offers information on the national consumption and cost of the medicines dispensed in Slovenian outpatient pharmacy; it does not cover hospital drug consumption and self-paid medicines. Ethical approval for the study was obtained from the National Medical Ethics Committee of the Republic of Slovenia in 2012.

Summary of results: In the age category 18-24 years, 16 patients were treated with MPH in 2013, 51 in 2008 and 76 in 2012; in the age category 25-49 years, the total number of treated patients with MPH increased from 12 in 2002 to 20 in 2012; in the age category >50 years, the total numbers were 5 (2003) and 6 (2012). In the age category 18-24 years, the total number of patients treated with ATX increased from 4 in 2008 to 12 in 2012; in the age category 25-49 years the total number of patients treated with ATX increased from 6 in 2008 to 12 in 2012. In patients over 50 years, 1 patient was treated in 2008 and 3 in 2012. In 2012 only 8.9% of ADHD patients treated were adults.

Conclusions: In the last decade in Slovenia the total number of treated patients with ADHD increased in all age categories, which indicates a positive trend, although many patients are still untreated. The low percentage of ADHD patients treated can be related to underdiagnosis, a lack of approved medications for adults with ADHD in Slovenia (IR-MPH, OROS-MPH), and gaps in the treatment between childhood and adulthood. In comparison with the results for children and adolescents with ADHD in Slovenia, it is evident that better cooperation between different levels of care is necessary to ensure appropriate treatment for all adults with ADHD

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DIFFERENCES IN UTILIZATION PATTERNS AMONG MEDICATIONS IN CHILDREN AND ADOLESCENTS WITH ATTENTION-DEFICIT HYPERACTIVITY DISORDER: A 36-MONTH NATURALISTIC RETROSPECTIVE STUDY USING THE KOREAN HEALTH INSURANCE REVIEW AND ASSESSMENT CLAIMS DATABASE.

Hwang JW, Bhang S, Kwack Y, et al.

Introduction: Suboptimal treatment and poor medication compliance were not uncommon even for 12 months of ADHD treatment [1]. In order to measure the adherence to long-term drug therapy retrospectively, analysis of prescription claims data has been used as a fairly reliable method. However, until now, the adherence to ADHD medication in several countries has been reported using the prescription claims data from either only selected populations or national representative samples with 1 year of less observation period [2,3].

Aims of the study: We evaluated the differences in utilization patterns including persistence and adherence among medications in children and adolescents with attention deficit hyperactivity disorder (ADHD).

Methods used: The current study was performed using data from the Korean Health Insurance Review and Assessment claims database from January 1, 2009 to December 31, 2013. Our study sample consisted of 10,343 children and adolescents with ADHD who were not given their newly prescribed medication in 360

days before the initial claim in 2010. Data were followed up from the initiation of treatment with ADHD medications in 2010 to December 31, 2013. Differences among ADHD medications in the number of those who discontinued and remained adherence were analyzed using chi-square test. Mean days before discontinuation were compared using ANOVA with post-hoc comparison. To assess the association between medications and persistence and adherence, a multivariate logistic regression analysis was employed, controlling for age, sex, and hospital level.

Summary of results: Discontinuation rates for 4 ADHD medications in our sample ranged from 97.7% for immediaterelease methylphenidate to 99.4% for atomoxetine using refill gap more than 30 days and from 56.7% for immediate-release methylphenidate to 62.3% for extended-release methylphenidate using refill gap more than 60 days. In the number of discontinued, we found significant differences among medications using refill gap more than 30 days (¤ç2 = 17.917, p<0.001). Among 4 ADHD medications, extended-release methylphenidate and atomoxetine had more days than immediate-release methylphenidate and osmotic-controlled oral delivery system methylphenidate. In logistic regression analyses, extended-release methylphenidate, osmotic-controlled oral delivery system methylphenidate, and atomoxetine showed less discontinuation compared to immediaterelease methylphenidate group when a refill gap more than 30 days was usedgroup [odds ratio (OR) = 0.528, 95% CI: 0.279- 0.996, p = 0.049; OR= 0.360, 95% CI: 0.203-0.639, p<0.001; OR= 0.270, 95% CI: 0.118-0.618, p = 0.002, respectively]. In logistic regression analysis of adherence, we could not find any differences among 4 medication types.

Conclusions: The results of the current study may contribute to add some evidences for effective adjustment of health care resources. Among Koreans, persistence and adherence varied depending on medication types, with IR-MPH having the lowest values. Overall adherence and persistence of ADHD medications in Korea were suboptimal. We suggest that the utilization patterns should be assessed regularly in order to improve future outcomes in children and adolescents with ADHD

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ARE AUTISTIC TRAITS IN YOUTH MEANINGFUL? A REPLICATION STUDY IN NON-REFERRED SIBLINGS OF YOUTH WITH AND WITHOUT ADHD.

Biederman J, Fried R, Joshi G.

Background: Recent studies showed that symptoms of autistic traits (ATs) appear in 20 to 30 percent of children with ADHD [1-3]. Children with ADHD and ATs appear to be more impaired and dysfunctional than children with ADHD and no ATs. Consistent with these findings in the literature, we assessed the prevalence and correlates of ATs in youth with and without ADHD, where a diagnosis of autism was exclusionary [4]. ATs were operationalized using a profile from the Child Behavior Checklist (CBCL) using extreme values from the sum of the Withdrawn, Social, and Thought Problems T-scores [5]. We previously reported on the high prevalence and burden of significant autistic traits (ATs) in youth with ADHD that is associated with significantly greater impairment in psychopathological, interpersonal, educational, and neuropsychological functioning. Because the sample consisted of referred ADHD youth, uncertainties remain as to whether these findings generalize to non-referred populations of youths with and without ADHD.

Objective: The main aim of the current study was to examine both the prevalence and correlates of ATs in non-referred youth with and without ADHD. To this end, we used data from an existing, large-scale sample of non-referred siblings of probands with and without ADHD. Based on the findings in probands, we hypothesized that ATs would be identifiable in non-referred siblings and that the presence of ATs would be associated with higher levels of morbidity and dysfunction.

Method: Participants were non-referred siblings of ADHD (N = 257) and Control (N = 234) probands of longitudinal, casecontrol family studies conducted at the Massachusetts General Hospital. Assessments included measures of psychiatric, psychosocial, educational, and cognitive functioning. Presence of significant ATs were operationalized using the Child Behavior Checklist (CBCL) AT profile consisting of an aggregate score ΓëÑ195 for the sum of the Withdrawn, Social, and Thought Problems T-scores.

Results: ATs were significantly more prevalent in siblings of ADHD probands compared to siblings of Control probands (6% vs. 1%, p = 0.02). Siblings of ADHD probands with a positive AT profile (N = 15) were significantly more impaired than those without an AT profile (N = 242) in psychopathological, interpersonal, educational, and neuropsychological functioning.

Conclusions: Consistent with previous findings on ATs in a referred sample of youth with ADHD, the current study reports a higher than expected prevalence of ATs in a non-referred sample of siblings of youth with ADHD. The present study shows that ATs can be identified in a sizeable minority of non-referred children, and that such children are at high risk for significant morbidity and disability. The current findings suggest that elevated scores on the CBCL-AT subscale may indicate a need to clinically assess for ASD, ADHD, mood, anxiety, and disruptive behavior disorders, emotional dysregulation, and impaired social and school functioning. These results provide further support for the clinical relevance of ATs irrespective of referral status

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METHYLPHENIDATE EFFECTS ON HEIGHT AND BONE AGE IN ADHD CHILDREN. 24 MONTH FOLLOW UP WITHIN THE PROSPECTIVE ADDUCE PROJECT.

Carucci S, Romaniello R, Lampis A, et al.

Background: In Europe methylphenidate (MPH) is the first choice medication for ADHD). Positive effects on the core symptoms are supported by numerous trials, but stimulants may induce several common mild and transient as well as rare and severe adverse events, including growth reduction with the prolonged use [1]. Several studies have monitored changes in growth during medication, providing inconclusive results on growth suppression induced by medication; only very few studies investigated the rate of bone age as a sensible parameter to predict a possible impact on height. Growing more slowly but continuing to have a bone maturation at the normal rate can in fact reflect the possibility of not reaching its own growth potential [2].

Objectives: To evaluate, within the prospective, longitudinal, pharmacovigilance, EU funded project ADDUCE, whether methylphenidate for ADHD is associated with a statistically significant increase in long-term risk of negative effects on height and bone maturation and to explore the application of monitoring of bone age as a helpful tool for studying adverse developmental effects.

Methods: Height, Weight, BMI, Target Height, X-ray of left wrist and the prediction of adult height were collected from 44 drug naïve ADHD Italian children, aged 6-12, at three time points: baseline visit and after 12 and 24 months.

Results: According to the Italian growth norms the 44 ADHD included into the study presented with a normal growth pattern at the baseline visit: height Z-score was 0.06±1.13, weight Z-score 0.11±1.21, BMI Z-score 0.12±1.17 and the Target Height Z-score for the male population was 0.26±0.92. The bone age calculated by the Tanner and Whitehouse II method was 8.07±2.10, resulting slightly behind the chronological age of 8.75±1.72 although not in a clinically significant manner. The 26 subjects retained into the study with a 24 month follow up presented with an adequate pattern of growth in terms of height (baseline Z score = 0.18±1.02 vs T24 Z score = 0.38±1.08) while BMI was slightly reduced after 24 months of treatment (baseline Z score = 0.14±1.16 vs T24 Z score = -0.04±1.22; p = 0.03). The bone age at the 24 month follow up time (10.97±2.18) was correctly aligned with the chronological age (10.85±1.69) evidencing a possible acceleration of bone maturation compared to the baseline measurements. The predicted adult height remained stable at each follow up time (baseline = 178.37±7.2; T12 = 177.18±7.8; T24 = 178.63±8.0).

Discussion: These results suggest that ADHD children present with a normal growth pattern in terms of height prior to starting medication and that this remains the case after 24 months of treatment. Medication may impact on weight during the first months of treatment with a significant reduction of BMI. The study of bone age indicated possible bone maturation acceleration, however the predicted adult height remained substantially stable at each follow up time indicating just a possible normalization of growth. Firm conclusions on the effects of medication on growth could be drawn only with a longer follow up at the reach of final height

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ATTENTION DEFICIT/HYPERACTIVITY DISORDER AND HANDWRITING: A KINEMATIC ANALYSIS.

Ivan-ìevi-ç N, Stevanovi-ç D, Miler Jerkovi-ç V, et al.

Background: The graphic rules and kinematic parameters are two main aspects assessed when determining handwriting difficulties [1]. The graphic rules include starting point rule, progression, and horizontal rule. With graphic rules can be predicted which movement is going to be used in handwriting task (e.g. writing a single letter or tracing simple shapes). The forces behind writing movements can be assessed with kinematics analysis (parameters). Kinematic parameters include velocity (V), pen tip pressure (P), acceleration (A), jerk (J), stroke duration (ST), stroke speed (SS), number of changes in velocity, and acceleration (NCV and NCA). It is suspected that difficulties with handwriting are very common among children with attention deficit/hyperactivity disorder (ADHD) [2]. The aim of this study was to evaluate the organization of the handwriting using graphic rules and kinematic parameters in children with ADHD compared to typically developed children (TDC).

Methods: Experimental study group included 15 right-handed boys (mean age 9.7±1.8 years) with ADHD. Six children were on methylphenidate treatment. Control group included 9 typically developing boys (all right-handed, mean age 10.1±0.2 years). All subjects performed the tracing task (in 3 repetitions) consisting of 4 semicircles rotated in clockwise direction by 90± on writing board by a stylus without a trace (Wacom Intuos4 XL, sampling rate 200 Hz, resolution 0.005 mm). Sampled data included starting point and the direction of the progression, with the mean values of earlier mentioned kinematic parameters.

Results: All subjects with ADHD did not differ to a greater extent from the controls in graphic rules; while the both groups even slighter deviated from these rules with each task repetition (see Table 1). The experimental and control group showed opposite trends during the task progression (from 1st/2nd to 4th semicircle) for all parameters except for the P value. Subjects from the experimental group wrote faster and more fluent with the task progression. Children with ADHD using methylphenidate significantly differed ($p<0.05$) from TDC regarding the V, A, J, ST and SS values. There were no statistically significant difference ($p>0.05$) between the groups in the mean values of the V, A, J, P, ST, SS, NCV and NCA.

Conclusion: Our results indicate that children with ADHD might differ from TDC in handwriting in the way that as a writing task progresses their handwriting becomes more organized, although they possibly have similar approach to a handwringing task. However, ADHD children treated with methylphenidate wrote similarly to TDC. Further research on a larger sample with different age, both genders and other presentations of ADHD is needed. (Table Presented)

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GENETIC DETERMINANTS OF METHYLPHENIDATE RESPONSE IN CHILDREN WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER.

Nemoda Z, Angyal N, Kruk E, et al.

Background: In the hope of personalized medicine, individual genetic variations influencing the pharmacokinetic properties and efficiency of the drug are studied. Methylphenidate (MPH) is the most frequently prescribed drug in the treatment of attention deficit hyperactivity disorder (ADHD). Hitherto, most of the ADHD pharmacogenetic studies focused on genetic variability at the drug targets, such as the dopamine transporter [1], and only a few analyzed genetic variants of metabolizing enzymes. In our previous study we reported that a functional single nucleotide polymorphism (SNP) in the carboxylesterase 1 gene (CES1), the Gly143Glu (rs71647871) can affect the metabolism of MPH [2]. However, the 143Glu variant was present only in 5.7% of the ADHD patients. Interestingly, there is copy number variation of this metabolizing enzyme gene but it does not seem to affect mRNA level or enzyme activity [3,4]. Therefore, we chose to study a more frequent promoter variant, the -75 A/C SNP (rs3815583 C-allele frequency is 18% in 1000 Genomes EUR population). In addition, the less-studied target molecule, the norepinephrine transporter (NET, SLC6A2) was analyzed in our prospective MPH-response study.

Methods: The patient group consisted of 122 Hungarian children with DSM-IV ADHD diagnosis (88.5% male, mean age: 9.6±2.6 SD). ADHD patients were given 10-30 mg MPH according to their body weight, in two doses (morning and noon), the average MPH dose was 0.55±0.15 mg/kg/day, ranging 0.22-0.95 mg/kg/day. The primary outcome measures of MPHtreatment were the ADHD-Rating Scale (at least 25% of total score

reduction was required for good response) and the Severity of Illness subscale of the Clinical Global Impression scale (CGI-S 0-2 scores, corresponding to no or minimal symptoms were required for good response). Using these cut-off scores resulted in 90 responders (73.8%) vs 32 non-responders (26.2%). In the dimensional approach repeated measures analyses of variance were carried out to test the effect of MPH on ADHD-RS subscales. Previously indicated SNPs of the CES1 gene (rs3815583) and the SLC6A2 gene (rs28386840, rs2242446, rs3785143, rs3785157, rs5569, rs7194256) were selected from different haplo-blocks, focusing on gene expression-relevant regions in the 5' and 3' UTRs.
Results: Homozygous carriers of the CES1-75 C-allele had better response in both the dimensional (ADHD-RS inattention, hyperactivity-impulsivity, and CGI-S scores $p < 0.05$) and categorical analyses ($p = 0.08$). Also the functional promoter variant of the SLC6A2 gene, the -3081 A/T SNP (rs28386840) showed association with MPH-response but only at the hyperactivityimpulsivity symptoms ($p = 0.04$) and not at the inattention symptoms ($p = 0.19$).
Conclusion: Although none of these genetic association findings remained significant after correcting for multiple testing, our results indicate that promoter variants in the metabolizing enzyme and target transporter genes might be worthwhile to study at the start of pharmacological treatment in ADHD. Importantly, not only dopamine but norepinephrine transporter should be taken into account at methylphenidate response evaluation

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LONG-TERM GROWTH-RELATED SAFETY OUTCOMES OF GUANFACINE EXTENDED RELEASE IN CHILDREN AND ADOLESCENTS WITH ADHD.

Huss M, Dirks B, Gu J, et al.

Introduction: Guanfacine extended release (GXR) is a nonstimulant treatment for attention-deficit/hyperactivity disorder (ADHD). In Europe, GXR is approved for children (6-12 years) and adolescents (13-17 years) with ADHD in whom stimulants are not suitable, not tolerated or have been shown to be ineffective. In the USA, GXR is indicated for the treatment of ADHD as monotherapy and as adjunctive therapy to stimulant medications. Here we report weight and height outcomes from study SPD503- 318, a phase 3 extension study assessing the long-term safety and efficacy of GXR in children and adolescents with ADHD.
Methods: SPD503-318 was an open-label, single-arm, extension study for European participants of the GXR clinical trials SPD503-315 [1] and SPD503-316 [2]. Dose-optimized GXR (1-7 mg/day) was administered once-daily for up to 2 years (7 weeks dose optimization; 95 weeks dose maintenance; 2 weeks taper). Participants who had received at least one dose of GXR were included in the safety population. Height and weight were assessed at baseline, during the dose maintenance and dose taper phases, and at follow-up. Final assessment was defined as the last valid assessment obtained after baseline whilst on investigational product and before dose taper. Based on body mass index (BMI), patients were categorized as underweight (<5th percentile), healthy weight (5th to <85th percentile), overweight (85th to <95th percentile) or obese (95th percentile).
Results: Of 215 enrolled participants, 214 (131 children; 83 adolescents) were included in the safety population. At baseline, the overall mean (standard deviation) height, weight, and BMI were 151.45(15.709) cm, 45.53(14.505) kg, and 19.32(2.900) kg/m2 respectively. Height-for-age, weight-for-age and BMI-for-age Z-scores at baseline and final assessment are shown in Table 1. At the final assessment, of 157 participants in the healthy weight category at baseline, 137 (87.3%) maintained a healthy weight, whereas 5 (3.2%) shifted to the underweight category, 14 (8.9%) to the overweight category and 1 participant (0.6%) shifted to the obese category. One child discontinued the study due to a treatment-emergent event of increased weight.
Conclusions: In children and adolescents with ADHD receiving GXR over two years, mean changes in height, weight and BMI were within the expected range of the included population. In small numbers of patients, prolonged GXR therapy may be associated with a shift to increased weight categories, highlighting the importance of regular weight monitoring during GXR treatment. (Table Presented)

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GENDER SPECIFIC DIFFERENCES IN AUDITORY BRAIN STEM RESPONSE IN YOUNG PATIENTS WITH ADHD.

Claesdotter-Hybbinette E, Cervin M, Akerlund S, et al.

Objective: The auditory brainstem response (ABR) is often affected in neurodevelopmental disorders [1-3]. The aim of this study was to investigate possible gender differences in ABR between young females and young males with ADHD, compared to control subjects.

Method: We studied 63 females with ADHD (mean 13.8 years, SD 2.5), 26 female controls (mean 13.8 years, SD 2.7), 48 males with ADHD (mean 13.1 years, SD 1.8), and 20 male controls (mean 12.8 years, SD 1.7). All patients were diagnosed according to the DSM-IV. The ABR consists of seven positive peaks (wave I-VII) that occur 10 ms following a stimulus recorded by five electrodes; one reference electrodes on the mastoid processes of each ear and two active electrodes and one ground electrode placed on the forehead.

Results: Comparing the ABR of 63 girls with ADHD to 26 age correlated control subjects 3 traits were identified, denoted TR6, TR14 and TR15. The higher value in TR6 ($p = 0.000064$), is explained by more aberrant curve profiles in the thalamic region. In TR14, the aberration was found in a region from superior olivary complex to thalamus ($p = 0.00059$). TR15 ($p = 0.00035$), is explained by more aberrant curve profiles in the lateral leminiscus. When looking at the ABR from 48 young males with ADHD and comparing them to 20 age correlated control subjects, we found 3 traits; TR4, TR5 and TR14. TR 4 is a lower correlation to a norm curve in inferior colliculus and thalamic area ($p = 0.00105$). TR5 identifies irregular curve profiles representing the nucleus cochlea ($p = 0.00027$). TR14, is described as an aberration in superior olivary complex to thalamus ($p = 0.00013$).

Conclusion: These data indicate both gender specific aberrations in the ABR in ADHD subjects as well as specific response differences between ADHD subjects and normal controls. Young females with ADHD exhibited a significantly different ABR in a region between cochlear nucleus and superior olivary complex and in the thalamic region. Neither of these differences could be seen in the male ADHD group when compared to the male control subjects. However, in the male ADHD group ABR aberrancy was found in the midbrain region and in the more peripheral part; nucleus cocleus. Only one trait was different for both male and females between the ADHD group and the control subjects. The present study suggests that the ABR method might provide useful biomarkers to support the clinical diagnoses of ADHD. Further studies of ABR and other child and adolescent disorders such as Autism and OCD are in progress. (Table Presented)

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PREVALENCE AND SYMPTOMATOLOGY OF ATTENTION DEFICIT HYPERACTIVITY DISORDER IN SCHOOL CHILDREN.

Gupta A.

Background: Attention Deficit Hyperactivity Disorder (ADHD) is the most common neurodevelopmental disorder among school age children [1]. It is frequently diagnosed in children with behavioural problems or in those who underachieve at school. Data from cross-sectional, retrospective and follow-up studies indicate that children with ADHD are at risk for developing other psychiatric disorders in childhood, adolescence and adulthood, such as antisocial behaviours, psychosis, alcoholism and substance abuse as well as depressive symptoms and depressive disorders [2].

Aim: This study was planned to identify ADHD children in schools of Ludhiana city and study their symptomatology. Method: A total of 2224 children were screened by the SNAPIV scale (teacher rating) for ADHD & Oppositional Defiant Disorder (ODD). A total of 78 children who were positive on this scale were called to the hospital for detailed assessment. Statistical significance was ascertained by z-tests, chi-square test (¤ç2) and rank correlation coefficient, as appropriate.

Results: A considerably high prevalence of ADHD was found in school going children (3.51%), more in boys (4.35%) than in girls (2.48%). In case of boys the maximum prevalence was in the 8 year age group i.e. 6.28%, followed by 7 years i.e. 4.24% and 6 years i.e. 2.63%. However, in case of girls, the prevalence of ADHD was maximum in the 7 year age group i.e. 3.43%. The most common subtype was the combined type followed by inattentive and hyperactive/impulsive type. Male sex and younger age predispose to predominantly hyperactive/impulsive type of disorder while female sex and older age predispose to predominantly inattentive type of disorder. ODD as co morbid to ADHD was more common in boys with increase in prevalence with increasing age. In general there is an increase in symptomatology with age but

in case of hyperactivity symptoms the 6 year olds outscored the 7 and 8 year olds. On all symptoms boys showed higher problematic behaviour and problem on more symptoms as compared to girls though frequency wise ranking of symptoms does not show any significant differences among the two (r-value significant). Academic underachievement was the most common associated problem affecting 65.30% of the children. Other associated problems included enuresis (28.75%), temper tantrums (22.4%), anxiety disorders (20.40%), ODD (16.32%), learning disorders (12.24%). A critical examination of the data showed that parents were more concerned about inattention and academic underperformance of their children while teachers viewed both inattention and hyperactivity as problematic.
Conclusions: ADHD has a considerably high prevalence among school age children. The impact of the disorder on society is enormous in terms of the financial cost, stress and the child's self esteem. Need of the hour is to spread awareness among caregivers regarding this debilitating disorder and formulation of effective management strategies

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SUBCLINICAL NON-EMOTIONAL ADHD SYMPTOMS ARE RELATED TO SMALLER CAUDAL ANTERIOR CINGULATE CORTEX VOLUME AND HIGHER IMPULSIVENESS.

Bayard F, Nymberg C, et al.

Introduction: Attention deficit hyperactivity disorder (ADHD) symptoms are normally distributed in the general population [1]. In clinical practice ADHD-symptoms may be divided into nonemotional symptoms (inattention/hyperactivity) and emotional dysregulation symptoms. Some brain regions, such as caudal anterior cingulate cortex (cACC) and dorsolateral prefrontal cortex (dlPFC), are involved in cognitive control of non-emotional processes, e.g. classical executive functions [2]. Other regions, including lateral orbitofrontal cortex (lObfc) and rostral anterior cingulate cortex (rACC), are involved in emotional regulation [3,4]. We hypothesized that subclinical symptoms related to non-emotional dysregulation would correlate negatively with cACC and dlPFC volume as well as non-emotional impulsivity control ability. Moreover, we hypothesized that subclinical symptoms related to emotional dysregulation would correlate negatively with lObfc and rACC volume and positively with tendency to discount the value of delayed rewards.
Aim: To investigate neural correlates of symptoms arising from dysfunctional non-emotional and emotional regulatory processes in healthy adolescents, and also connect these symptoms to behavioral measurements.
Methods: Healthy 14-year-old adolescents (n = 1124) from the European multi-center IMAGEN study were included in this study [5]. Participants went through MRI scanning as well as extensive neuropsychological assessment. For behavioral measurements we used parts of the Strength and Difficulties Questionnaire (SDQ), the Stop Signal Reaction Time (SSRT) from the Stop Signal Task (measurement of impulsivity control) and an estimated delay discounting coefficient from a questionnaire (reflecting tendency to discount a delayed reward). We focused on four cortical ROIs: dlPFC, lObfc, cACC and rACC as obtained by Freesurfer. R, version 3.1.3 and QDEC provided by Freesurfer, version 5.0, were used for analyses. Gender and imaging center were controlled for in all the analyses.
Results: All ROI volumes correlated negatively with the nonemotional Hyperactivity SDQ score, while only the dlPFC and rACC volumes correlated negatively with the emotionally related combined Emotion/Conduct SDQ score. To obtain the unique contribution to the correlation of each SDQ subscale the same analyses were performed, controlling for the other subscales. Both the cACC volume (±=-0.087, p<0.01) and the lObfc volume (± =-0.098, p<0.001) correlated negatively with Hyperactivity SDQ score, when controlling for Emotion/Conduct SDQ score. None of the predefined ROI volumes correlated significantly with Emotion/Conduct SDQ score when controlling for Hyperactivity SDQ score, although a trend effect was observed in rACC (b =-0.057, p = 0.083). SSRT correlated positively with Hyperactivity SDQ score (± = 0.11, p<0.05) when controlling for Emotion/Conduct SDQ score. The delay discounting coefficient correlated with the Conduct SDQ subscale score (+¦ = 0.010, p<0.01) when controlling for the other SDQ subscale scores.
Conclusions: A smaller cACC volume, and a larger inability to control impulsivity, were associated with higher Hyperactivity SDQ scores in healthy 14-year olds even when controlling for emotional dysregulation. This result partly strengthens our hypothesis of a non-emotional regulatory system coupled to behavioral measurements of non-emotional problems. The tendency to discount the value of a delayed reward was

associated with conduct problems. These results are in line with the hypothesis that non-emotional and emotional problems in healthy adolescents have partly different neurobiological basis that may be coupled to specific behavioral measurements

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Eur Neuropsychopharmacol. 2016;26:S149.

THE DEVELOPMENT OF THE CLINICAL PRESENTATION OF ADHD THROUGH THE LIFESPAN.

Reif A.

Classically, attention deficit / hyperactivity disorder (ADHD) was considered a childhood condition which then wanes during adolescence. In the last 25 years, this concept was challenged and it is meanwhile well appreciated that ADHD can also be an adulthood conditions, with about 50% of affected children continue to have symptoms in adulthood and another 15% still suffer from the full syndrome. One factor that has obscured the identification of adult ADHD is the marked change in the clinical presentation of the disorder. Hyperactivity, being a hallmark of ADHD in childhood, in most cases is no longer a major problem in adulthood; attention deficits can often be coped with well by adults, depending in their environmental demands. On the other hands, emotional dysregulation and mood disturbances become more and more predominant, the older the patients get. Also substance use disorder play in important role along the developmental trajectory. To complicate matters even further, ADHD goes along with a high rate of comorbid conditions and these as well change considerably over the life span. Gender effects have an important role as well, which is reflected by different prevalence rates of ADHD in both sexes in childhood as compared to adulthood. This review talk will summarize the present knowledge about changes in the clinical presentation of ADHD over the life span, and highlight the diagnostic and therapeutic challenges that go along with it

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EFFICACY OF ATOMOXETINE IN CHILDREN AND ADOLESCENTS WITH ATTENTION DEFICIT/ HYPERACTIVITY DISORDER.

Yamamuro K, Ueda J, Takada R, et al.

Attention-deficit hyperactivity disorder (ADHD) is characterized by inattention, hyperactivity, impulsively, and abnormalities in one or more cognitive processes. ADHD is a serious psychological disorder that occurs in 3 to 7% of the global population [1,2]. The psychostimulant methylphenidate (MPH) and the selective norepinephrine reuptake inhibitor atomoxetine (ATX) are commonly used for treatment of ADHD symptoms. However, there are few biological indicators of their pharmacological effects. Eventrelated potentials (ERPs) are commonly used as a non-invasive physiological measure of cognitive dysfunction associated with several psychiatric disorders, including ADHD [3], obsessivecompulsive disorder (OCD) [4] and at-risk mental state [5]. Also, ERPs is commonly used as physiological measures to explore the underlying neurophysiological mechanisms and characteristics of cognitive dysfunctions in several psychiatric disorders, including ADHD. Few objective biological measures of the efficacy of pharmacological treatments for attention deficit/hyperactivity disorder (ADHD) exist. The psychostimulant methylphenidate (MPH) and the selective norepinephrine reuptake inhibitor atomoxetine (ATX) are commonly used for treatment of ADHD symptoms. We previously demonstrated the effects of osmotic-release MPH in treatment naïve pediatric patients with ADHD, as measured by ERPs. However, whether ERPs reflect the therapeutic effects of ATX is unknown. We used the ADHD rating scale-IV-Japanese version to evaluate 14 patients with ADHD. Present study also included 14 age- and sex-matched controls. We confirmed the absence of a psychiatric diagnosis in control group using a standard clinical assessment that included a psychiatric evaluation and a structured diagnostic interview (Structured Clinical Interview for DSM-IV Axis Disorders Non-Patient Edition; SCIS-NP). All patients, who were right-handed and of Japanese descent, were diagnosed with ADHD according to the DSM-IV-R. All participants and/or their caregivers provided written informed consent for their participation in the study. This study was approved by the Institutional Review Board at the Nara Medical University. We measured P300 and mismatch negativity (MMN) components during an auditory odd-ball task in a treatment naïve condition and 2 months after initiation of ATX treatment. Compared with controls, the P300 components was attenuated and prolonged in the treatment group at Fz (fronto-central), Cz (centro-parietal), Pz (parietal

regions), C3 and C4 at baseline. We conducted a statistical comparison of participant characteristics in the two groups using a twotailed paired t-test. We compared the latencies and amplitudes of both the P300 and MMN components before vs. after treatment using a two-tailed paired t-test. We used PASW Statistics 18.0 J for Windows (SPSS, Tokyo, Japan) for the statistical analyses. ATX reduced ADHD symptomology. P300 latencies after onset of ATX treatment were significantly shorter than those at baseline at Fz, Cz, Pz, C3, and C4. Moreover, MMN amplitudes were significantly greater than those at baseline at Cz and C3. ERPs may have potential in evaluating the pharmacological effects of ATX in pediatric and adolescent patients with ADHD

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Eur Neuropsychopharmacol. 2016;26:S717.

THE THEORY OF MIND AND SOCIAL FUNCTIONALITY IN PATIENTS WITH ATTENTION DEFICIT DISORDERHYPERACTIVITY DISORDER.

Romero Guillena SL, Rodriguez Gravan V, et al.

Introduction: Patients with schizophrenia, bipolar disorder or autism are known to develop theory of Mind (ToM) impairments [1]. Research on the theory of mind in children with attention deficit disorder/hyperactivity disorder (ADHD) has demonstrated the existence of significant differences between ADHD patients and controls such as a poorer performance of ADHD patients in false belief attribution and pragmatic language tasks. In contrast, no significant differences have been observed in performance in the Reading the Mind in the Eyes Test. Thus, there is evidence supporting that ToM may account for the differences observed in social skills between ADHD children and controls [2].

Objectives: The main goal of this study was to determine a potential impairment in the emotional component of ToM in patients with ADHD. The secondary objective was to assess the potential relationship between the ToM and social functioning in ADHD children.

Materials and Methods: The sample was composed of 25 patients diagnosed with attention deficit disorder/hyperactivity disorder (ADHD) aged 6 to 17 years. During the study, patients received drug therapy and psychotherapeutic treatment. The group of controls was composed of 25 subjects without any psychiatric disorder. Inter-group subjects were matched by age, gender and years of education. The emotional component of ToM was assessed using the Reading the Mind in the Eyes Test version for children (REMET). The test comprises 28 black and white pictures of the eyes of male and female faces expressing different states of mind. The subject is asked to choose between four emotion terms the one that best expresses the state of mind of the eyes of the picture. Social functioning was assessed using the WFIRS scale (Weiss Functional Impairment Rating Scale) ('Social Activities' domain). The data obtained were analyzed using the SPSS 20.0 statistical package. A level of confidence >95% was considered statistically significant. Mean values for quantitative variables were compared using Student's t-test for independent groups (parametric test). Pearson's correlation coefficient was calculated to determine the correlation between REMET and WFIRS. A linear regression model was constructed using REMET as the dependent variable and WFIRS as a potential predictor.

Results: Sample: ADHD Group (N = 25; gender: 80% males and 20% females; age: 11.80 (± 2.59). Controls (N = 25; gender: 80% males and 20% females; age: 11.42 (± 2.65). No statistically significant differences were observed by gender, age or years of education. The mean score on the Eyes test was significantly lower in ADHD patients, as compared to controls, 16.80 vs. 20.13 (I.C. 95%: -5.12; -1.44), P<0.001. A strong, inverse, linear correlation (r = -0.748; p<0.001) was observed between REMET and WFIRS (social activities domain) scores. Scores on the Eyes Test would account for 56% of variability in WFIRS scores (b1= -1.52; C.I. 95%= (-2.11, -0.94)).

Conclusions: In contrast with the results reported in previous studies, the performance of patients with ADHD in the emotional component of ToM is significantly poorer, as evidenced by lower scores on the Eyes Test. There is a strong correlation between social functioning and the emotional component of Theory of Mind. Further studies should be conducted to assess the correlations observed in this study more thoroughly

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Eur Neuropsychopharmacol. 2016;26:S721-S722.

THE ASSOCIATION BETWEEN EARLY CHILDHOOD ONSET EPILEPSY AND COMORBID AUTISM-ADHD: A PROSPECTIVE STUDY OF 3032 CHILDREN WITH AUTISM SPECTRUM DISORDERS.

Downs J, Safa T, Owen-Philips J, et al.

Background: Over 1 in 4 children with Autism Spectrum Disorders (ASD) present to mental health services with comorbid symptoms of Attention Deficit Hyperactivity Disorders (ADHD) [1]. Several studies describe overlapping genetic and cognitive profiles which suggest shared aetiological pathways for ASD and ADHD [2]. Yet, there are very few prospective studies that generate and test candidate risk factors for ADHD and ASD co-occurrence. We propose that early childhood onset epilepsy may be prospectively associated with ASD-ADHD comorbidity. Childhood ASD is strongly associated with epilepsy [3], whilst childhood epilepsy is prospectively associated with ADHD [4]. Whether children with ASD, who also experience early childhood epilepsy, are at elevated risk for ADHD co-occurrence remains unclear.

Aim: To use linked acute physical and mental health paediatric records to conduct a historical cohort study in large sample of children with ASD, and examine the prospective association between early childhood onset epilepsy (under 7 years old) and co-morbid ADHD development.

Methods: Data were obtained from a cohort of 3032 children (78% male) with ASD, referred between the ages of 3 and 17 to child and adolescent mental health services (CAMHS) in South London, UK. ICD-10 Diagnoses for epilepsy disorders, disorders associated with symptomatic epilepsy (i.e. acquired disorders or those of predominately genetic/ developmental causation), and ADHD were extracted from electronic patient records using the Clinical Record Interactive Search (CRIS) system linked to national Hospital Episode Statistics. Using logistic regression, the prospective association between early childhood onset epilepsy and ADHD outcomes were examined over a 5-year follow period.

Results: Of the 3032 children with ASD, 114 children (3.76%) had a record of early childhood onset epilepsy and 773 (25.5%) were diagnosed with co-morbid ADHD by CAMHS within the follow up period. We identified a significant association between early childhood onset epilepsy in ASD and developing co-occurring ADHD (adjusted odds ratio 1.75; 95% CI 1.13- 2.71; p = 0.01) which persisted after controlling for potential confounders including socio-demographic factors, intellectual disability, early childhood onset symptomatic epilepsy disorders, and family history of epilepsy. We found male gender (aOR 1.67: 95% CI 1.33-2.12; p<0.01) and presence of any early childhood symptomatic epilepsy disorders (aOR 1.42; 1.25-1.81, p<0.01) were positively associated with ADHD co-occurrence. Compared to white ethnic groups, black (aOR 0.63: 95% CI 0.49- 0.80; p<0.01) and asian (aOR 0.48: 95% CI 0.29-0.58; p<0.01) groups were negatively associated.

Conclusion: For children with ASD, early childhood onset epilepsy contributes significant risk for ADHD. Our findings suggest that early childhood epilepsy may represent a risk factor on a shared causal path for ASD and ADHD. Further work is needed to elucidate whether conventional approaches to ADHD management have the same risk benefit profiles within early childhood onset epilepsy-ASD subgroups

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Expert Rev Neurother. 2017;17:113-21.

THE USE OF MODIFIED-RELEASE METHYLPHENIDATE IN THE TREATMENT OF ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.

Childress A, Belchenko D, Lempa B.

Introduction: Since Ritalin (Methylphenidate-Immediate release or MPH-IR) was introduced for the treatment of attention-deficit/hyperactivity disorder, multiple formulations of MPH have been developed. The specific formulation determines the pharmacokinetic (PK) profile and the onset and duration of action for the compound.

Areas covered: Aptensio XR is a multilayer-release MPH (MPH-MLR) consisting of an MPH-IR layer (40%) and an extended-release (ER) portion of 60% of MPH. It has an initial maximum MPH concentration at about two hours (h) and a second concentration peak at approximately 8-h. This formulation allows for a rapid onset of effect by 1-h and a duration of action through 12-h after dosing. The chemistry, PK, efficacy and adverse event profile of MPH-MLR will be reviewed.

Expert commentary: Although the PK profile may prove beneficial to patients in the late afternoon and early evening, it is not clear if this is a significant advantage compared with other MPH-ER formulations

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International Journal of Developmental Disabilities. 2017;63:27-35.

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

Climie EA, Mitchell K.

Objectives: Previous studies have examined the effect of parent–child relationships on conduct problems, but rarely are the mother–child and father–child relationships studied independently. The current study examined parent–child relationships and their connection to comorbid behaviors in children with Attention-Deficit/Hyperactivity Disorder (ADHD). More specifically, this study explored the mother–child and father–child relationship in children with ADHD, with an explicit focus on the aspects of the parent–child relationship that are related to more positive behavioral outcomes.
Methods: A sample of 74 children with ADHD (aged 8–11 years) and their mothers (n = 74) and fathers (n = 37) participated in the current study and completed a variety of parenting and behavioral measures. A number of relationship factors, including parent- and child-reported levels of attachment were examined in connection to parental ratings of behavioral outcomes such as defiance, aggression, and conduct problems.
Results: Results indicated that different aspects of the parent–child relationship for mothers and fathers were related to ratings of behavioral problems. Relational frustration was found to be a consistent predictor of negative ratings of behavior for both parents, while involvement was a predictor of more positive ratings of behavior for fathers only.
Conclusions: A better understanding of the specific aspects of the mother–child and father–child relationship may play a role in helping to understand the link between parent–child relationships and behavioral concerns in children with ADHD. Implications for practice are highlighted with a particular emphasis on strengthening the parent–child bond in families with children with ADHD.

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J Child Adolesc Psychopharmacol. 2016 Mar;26:101-06.

DISRUPTIVE MOOD DYSREGULATION DISORDER SYMPTOMS AND ASSOCIATION WITH OPPOSITIONAL DEFIANT AND OTHER DISORDERS IN A GENERAL POPULATION CHILD SAMPLE.

Mayes SD, Waxmonsky JD, Calhoun SL, et al.

OBJECTIVE: The new Diagnostic and Statistical Manual of Mental Disorders, 5th ed. (DSM-5) diagnosis, disruptive mood dysregulation disorder (DMDD), has generated appreciable controversy since its inception, primarily in regard to its validity as a distinct disorder from oppositional defiant disorder (ODD). The goal of our study was to determine if the two DSM-5 DMDD symptoms (persistently irritable or angry mood and severe recurrent temper outbursts) occurred independently of other disorders, particularly ODD. Other DSM-5 DMDD criteria were not assessed.
METHODS: Maternal ratings of the two DMDD symptoms, clinical diagnosis of ODD using DSM-5 symptom criteria, and psychological problem scores (anxiety, depression, oppositional behavior, conduct disorder, and attention-deficit/hyperactivity disorder [ADHD]) on the Pediatric Behavior Scale were analyzed in a population sample, 6-12 years of age (n = 665).
RESULTS: The prevalence of DMDD symptoms (irritable-angry mood and temper outbursts both rated by mothers as often or very often a problem) was 9%. In all, 92% of children with DMDD symptoms had ODD, and 66% of children with ODD had DMDD symptoms, indicating that it is very unlikely to have DMDD symptoms without ODD, but that ODD can occur without DMDD symptoms. Comorbid psychological problems (anxiety, depression, conduct disorder, and ADHD) in addition to ODD did not increase the risk of having DMDD symptoms beyond that for ODD alone. Only 3% of children with psychological problems other than ODD had DMDD symptoms.
CONCLUSIONS: Our general population findings are similar to those for a psychiatric sample, suggesting that DMDD cannot be differentiated from ODD based on symptomatology. Therefore, it is important to assess all DSM criteria and to examine for comorbid psychopathology when considering a diagnosis of DMDD. Our

results support the recommendation made by the World Health Organization's International Classification of Diseases, 11th Revision (ICD-11) panel of experts that DMDD symptoms may be more appropriately classified as an ODD specifier than a separate diagnosis

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J Child Adolesc Psychopharmacol. 2016 Mar;26:147-53.

PREVALENCE AND CORRELATES OF DISRUPTIVE MOOD DYSREGULATION DISORDER AMONG ADOLESCENTS WITH BIPOLAR DISORDER.

Mitchell RH, Timmins V, Collins J, et al.

OBJECTIVE: The purpose of this study was to examine the prevalence and correlates of disruptive mood dysregulation disorder phenotype (DMDDP) in a clinical population of adolescents with bipolar disorder (BD).
METHODS: DMDD criteria were modified and applied to a sample of 116 adolescents with BD-I (n = 30), BD-II (n = 46) or BD-not otherwise specified (NOS) (n = 40) from a tertiary teaching hospital. Diagnoses were determined via the Kiddie Schedule for Affective Disorders and Schizophrenia for School-Aged Children, Present and Lifetime version (KSADS-PL). Diagnostic and Statistical Manual of Mental Disorders (DSM-5) DMDD Criteria A-G were derived from the KSADS oppositional defiant disorder (ODD) screening interview and supplement, as well as narrative summaries. Chi-square analyses or t tests ($p < 0.05$) were conducted as appropriate, followed by logistic regression. P values were adjusted using the false discovery rate (FDR) approach.
RESULTS: DMDDP criteria could not be determined for 8 adolescents because of missing data from the ODD supplement. Twenty-five percent of the remainder (27/108) met criteria for DMDDP. DMDDP was not associated with BD subtype or with family history of BD. In univariate analyses, after controlling for age, sex, and race, DMDDP was associated with lower functioning, increased family conflict, assault history, and attention deficit and/or hyperactivity disorder (ADHD) (FDR adjusted p values: <0.0001, < 0.0001, 0.007, and 0.007, respectively). Lifetime substance use disorder and medication use approached significance (adjusted $p = 0.05$). In logistic regression, DMDDP was independently associated with greater parent-reported family conflict (odds ratio [OR] 1.17; confidence interval [CI- 1.06-1.30; $p = 0.001$) and greater functional impairment (OR 0.89; CI 0.82-0.97; $p = 0.006$). DMDDP was also associated with a threefold increase in ADHD, although ADHD was only marginally significant (OR 3.3; CI 0.98-10.94; $p = 0.05$).
CONCLUSIONS: Despite the positioning of DMDD as phenotypically and biologically distinct from BD, these phenotypes commonly overlap in clinical settings. This overlap is not explained by BD-NOS or by nonfamilial BD. The association of ADHD with DMDDP in this sample draws into question whether arousal symptoms should have been retained as originally elaborated in the severe mood dysregulation phenotype. Strategies to mitigate the excessive functional impairment of this comorbidity are warranted

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J Child Adolesc Psychopharmacol. 2016 Mar;26:123-30.

DISRUPTIVE MOOD DYSREGULATION DISORDER IN A COMMUNITY MENTAL HEALTH CLINIC: PREVALENCE, COMORBIDITY AND CORRELATES.

Freeman AJ, Youngstrom EA, Youngstrom JK, et al.

OBJECTIVE: The revision of the Diagnostic and Statistical Manual of Mental Disorders, 5th ed. (DSM-5) added a new diagnosis of disruptive mood dysregulation disorder (DMDD) to depressive disorders. This study examines the prevalence, comorbidity, and correlates of the new disorder, with a particular focus on its overlap with oppositional defiant disorder (ODD), with which DMDD shares core symptoms.
METHODS: Data were obtained from 597 youth 6-18 years of age who participated in a systematic assessment of symptoms offered to all intakes at a community mental health center (sample accrued from July 2003 to March 2008). Assessment included diagnostic, symptomatic, and functional measures. DMDD was diagnosed using a post-hoc definition from item-level ratings on the Schedule for Affective Disorders and Schizophrenia for School-Age Children that closely matches the DSM-5 definition. Caregivers rated youth on the Child Behavior Checklist.

RESULTS: Approximately 31% of youth met the operational definition of DMDD, and 40% had Diagnostic and Statistical Manual of Mental Disorders, 4th ed. (DSM-IV) diagnoses of ODD. Youth with DMDD almost always had ODD (odds ratio [OR] = 53.84) and displayed higher rates of comorbidity with attention-deficit/hyperactivity disorder (ADHD) and conduct disorder than youth without DMDD. Caregivers of youth with DMDD reported more symptoms of aggressive behavior, rule-breaking, social problems, anxiety/depression, attention problems, and thought problems than all other youth without DMDD. Compared with youth with ODD, youth with DMDD were not significantly different in terms of categorical or dimensional approaches to comorbidity and impairment.
CONCLUSIONS: The new diagnosis of DMDD might be common in community mental health clinics. Youth with DMDD displayed more severe symptoms and poorer functioning than youth without DMDD. However, DMDD almost entirely overlaps with ODD and youth with DMDD were not significantly different than youth with ODD. These findings raise concerns about the potentially confusing effects of using DMDD in clinical settings, particularly given that DSM-5 groups DMDD with depressive disorders, but ODD remains a disruptive behavior disorder, potentially changing the decision-making framework that clinicians use to select treatments

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J Child Adolesc Psychopharmacol. 2016 Mar;26:181.
REPORT OF A 14-YEAR-OLD BOY WHOSE TESTOSTERONE LEVEL DECREASED AFTER STARTING ON METHYLPHENIDATE.
Akaltun I.

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J Child Neurol. 2016 May;31:750-60.
EFFECTS OF SMART-TABLET-BASED NEUROFEEDBACK TRAINING ON COGNITIVE FUNCTION IN CHILDREN WITH ATTENTION PROBLEMS.
Shin MS, Jeon H, Kim M, et al.
We sought to determine whether smart-tablet-based neurofeedback could improve executive function-including attention, working memory, and self-regulation-in children with attention problems. Forty children (10-12 years old) with attention problems, as determined by ratings on the Conners Parent Rating Scale, were assigned to either a neurofeedback group that received 16 sessions or a control group. A comprehensive test battery that assessed general intelligence, visual and auditory attention, attentional shifting, response inhibition and behavior rating scales were administered to both groups before neurofeedback training. Several neuropsychological tests were conducted at posttraining and follow-up assessment. Scores on several neuropsychological tests and parent behavior rating scales showed significant improvement in the training group but not in the controls. The improvements remained through the follow-up assessment. This study suggests that the smart-tablet-based neurofeedback training program might improve cognitive function in children with attention problems

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J Child Psychol Psychiatry. 2016 Apr;57:443-45.
EXECUTIVE FUNCTIONING - A KEY CONSTRUCT FOR UNDERSTANDING DEVELOPMENTAL PSYCHOPATHOLOGY OR A 'CATCH-ALL' TERM IN NEED OF SOME RETHINKING?
Halperin JM.
For the past few decades, the role of executive functions in developmental psychopathology has been the focus of considerable research and a feature of conceptual models for a range of conditions including, but not limited to, ADHD, autism, schizophrenia, bipolar disorder, learning disorders, and aggression/conduct problems. Consistent with its prominence throughout the field, executive functioning plays a central role in approximately a third of the papers in this issue of JCPP, and notably, with foci largely on different conditions.

These papers, all of which make valuable contributions to the field, propose or test the possibility of a causal role for executive functions in the emergence of psychopathology

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J Clin Psychopharmacol. 2016 Jun;36:262-71.

A Prospective Open-Label Trial of Memantine Hydrochloride for the Treatment of Social Deficits in Intellectually Capable Adults With Autism Spectrum Disorder.

Joshi G, Wozniak J, Faraone SV, et al.

This prospective 12-week open-label trial evaluates the tolerability and efficacy of memantine hydrochloride for the treatment of core social and cognitive deficits in adults with high-functioning autism spectrum disorder (ASD). Measures for assessment of therapeutic response included the Social Responsiveness Scale-Adult Research Version (SRS-A), disorder-specific Clinical Global Impression scales, Behavior Rating Inventory of Executive Functioning-Adult Self-Report, Diagnostic Analysis of Nonverbal Accuracy Scale, and Cambridge Neuropsychological Test Automated Battery. Eighteen adults (mean age, 28 +/- 9.5 years) with high-functioning ASD (SRS-A raw score, 99 +/- 17) were treated with memantine (mean dose, 19.7 +/- 1.2 mg/d; range, 15-20 mg), and 17 (94%) completed the trial. Treatment with memantine was associated with significant reduction on informant-rated (SRS-A, -28 +/- 25; P < 0.001) and clinician-rated (Clinical Global Impression-Improvement subscale </=2, 83%) measures of autism severity. In addition, memantine treatment was associated with significant improvement in ADHD and anxiety symptom severity. Significant improvement was noted in nonverbal communication on the Diagnostic Analysis of Nonverbal Accuracy Scale test and in executive function per self-report (Behavior Rating Inventory of Executive Functioning-Adult Self-Report Global Executive Composite, -6 +/- 8.8; P < 0.015) and neuropsychological assessments (Cambridge Neuropsychological Test Automated Battery). Memantine treatment was generally well tolerated and was not associated with any serious adverse events. Treatment with memantine appears to be beneficial for the treatment of ASD and associated psychopathology and cognitive dysfunction in intellectually capable adults. Future placebo-controlled trials are warranted

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J Clin Psychopharmacol. 2016 Jun;36:222-28.

Factors Associated With Adherence to Methylphenidate Treatment in Adult Patients With Attention-Deficit/Hyperactivity Disorder and Substance Use Disorders.

Skoglund C, Brandt L, Almqvist C, et al.

Adherence to treatment is one of the most consistent factors associated with a favorable addiction treatment outcome. Little is known about factors associated with treatment adherence in individuals affected with comorbid attention-deficit/hyperactivity disorder and substance use disorders (SUD). This study aimed to explore whether treatment-associated factors, such as the prescribing physician's (sub)specialty and methylphenidate (MPH) dose, or patient-related factors, such as sex, age, SUD subtype, and psychiatric comorbidity, were associated with adherence to MPH treatment. Swedish national registers were used to identify adult individuals with prescriptions of MPH and medications specifically used in the treatment of SUD or a diagnosis of SUD and/or coexisting psychiatric diagnoses. Primary outcome measure was days in active MPH treatment in stratified dose groups (</=36 mg, >/=37 mg to </=54 mg, >/=55 mg to </=72 mg, >/=73 mg to </=90 mg, >/=91 mg to </=108 mg, and >/=109 mg). Lower MPH doses (ie, </=36 mg day 100) were associated with treatment discontinuation between days 101 and 830 (HR</=36 mg, 1.67; HR37-54mg, 1.37; HR55-72mg, 1.36; HR73-90mg, 1.19; HR>/=108mg, 1.09). The results showed a linear trend (P < 0.0001) toward decreased risk of treatment discontinuation along with increase of MPH doses. In conclusion, this study shows that higher MPH doses were associated with long-term treatment adherence in individuals with attention-deficit/hyperactivity disorder and SUD

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J Consult Clin Psychol. 2016 May;84:465-71.

LONG-TERM OUTCOMES OF BRIEF, INTENSIVE CBT FOR SPECIFIC PHOBIAS: THE NEGATIVE IMPACT OF ADHD SYMPTOMS.

Halldorsdottir T, Ollendick TH.

OBJECTIVES: The objectives were twofold: (a) examine long-term treatment effects in youth receiving 1-session treatment (OST) or educational support (EST) for a specific phobia (SP) and (b) examine the differential predictive and moderation effects of attention-deficit/hyperactivity disorder (ADHD) symptoms on immediate and long-term outcomes following the interventions.

METHOD: Eighty-three children (ages 6-15, 47% female, 89% White) with a SP were randomly assigned to receive OST or EST. Follow up assessments occurred at 1 week, 6 months, 1 year, and 4 years. Hierarchical linear growth modeling (HLGM) was used to explore the association of parent-reported ADHD symptoms, the 2 treatment conditions (i.e., OST vs. EST), and the trajectory of change in the severity of the SP from pretreatment to the 4-year follow-up. Age, conduct problems and learning problems were controlled for in all analyses.

RESULTS: A greater immediate reduction in severity rating of the SP was observed in the OST compared to EST, whereas the trajectory of long-term outcomes was similar across conditions over time. Higher levels of ADHD symptoms predicted poor immediate and long-term treatment outcomes across treatment conditions. ADHD symptoms, however, did not moderate the relationship between treatment condition and immediate or long-term treatment outcomes.

CONCLUSIONS: The results of the study need to be interpreted in light of several study limitations. However, if confirmed, the findings suggest that anxious youth with comorbid ADHD symptoms are less likely to benefit from brief, intensive psychotherapy and may require either longer, standard CBT treatment or adjunctive pharmacotherapy

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J Health Soc Behav. 2015 Sep;56:415.

JHSB POLICY BRIEF. DOES MEDICAL TREATMENT OF CHILDREN'S BEHAVIORAL PROBLEMS LOWER FOSTER CARE RATES?

Fallesen P, Wildeman C.

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J Korean Med Sci. 2016 Apr;31:611-16.

NATURALISTIC PHARMACOTHERAPY COMPLIANCE AMONG PEDIATRIC PATIENTS WITH ATTENTION DEFICIT/HYPERACTIVITY DISORDER: A STUDY BASED ON THREE-YEAR NATIONWIDE DATA.

Hong M, Kim B, Hwang JW, et al.

We examined short- and long-term medication compliance among youth with attention-deficit hyperactivity disorder (ADHD), using data from the National Health Insurance database in Korea. Of the 5,699,202 6-14-year-old youth in 2008, we chose those with at least 1 medical claim containing an ICD-10 code for diagnosis of ADHD (F90.0) and no prescription for ADHD within the previous 365 days. We tracked the data every 6 months between 2008 and 2011, to determine treatment compliance among newly diagnosed, medicated patients. Further, we checked every 1 month of the 6 months after treatment commencement. Treatment continuity for each patient was calculated by sequentially counting the continuous prescriptions. For measuring compliance, we applied the medication possession ratio (MPR) as 0.6, 0.7, and 0.8, and the gap method as 15- and 30-days' intervals. There were 15,133 subjects; 11,934 (78.86%) were boys. Overall 6-month treatment compliance was 59.0%, 47.3%, 39.9%, 34.1%, 28.6%, and 23.1%. Monthly drop-out rates within the first 6 months were 20.6%, 6.5%, 4.7%, 3.7%, 3.0%, and 2.5%, respectively. When applying MPR more strictly or shorter gap days, treatment compliance lessened. This is the first nationwide report on 36-month treatment compliance of the whole population of 6-14-year-olds with ADHD. We found the beginning of the treatment, especially the first month, to be a critical period in pharmacotherapy. These results also

suggest the importance of setting appropriate treatment adherence standards for patients with ADHD, considering the chronic course of ADHD

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J Ment Health Policy Econ. 2016 Jun;19:91-101.

DOES PREVENTION PAY? COSTS AND POTENTIAL COST-SAVINGS OF SCHOOL INTERVENTIONS TARGETING CHILDREN WITH MENTAL HEALTH PROBLEMS.

Wellander L, Wells MB, Feldman I.

In Sweden, the local government is responsible for funding schools in their district. One funding initiative is for schools to provide students with mental health problems with additional support via extra teachers, personal assistants, and special education classes. There are evidence-based preventive interventions delivered in schools, which have been shown to decrease the levels of students' mental health problems. However, little is known about how much the local government currently spends on students' mental health support and if evidence-based interventions could be financially beneficial. The aim of this study was to estimate the costs of providing additional support for students' mental health problems and the potential cost-offsets, defined as reduced school-based additional support, if two evidence-based school interventions targeting children's mental health problems were implemented in routine practice. This study uses data on the additional support students with mental health problems received in schools. Data was collected from one school district for students aged 6 to 16 years. We modeled two Swedish school interventions, Comet for Teachers and Social and Emotional Training (SET), which both had evidence of reducing mental health problems. We used a cost-offset analysis framework, assuming both interventions were fully implemented throughout the whole school district. Based on the published studies, the expected effects and the costs of the interventions were calculated. We defined the cost-offsets as the amount of predicted averted additional support for students with ongoing mental health problems who might no longer require receiving services such as one-on-one time with an extra teacher, a personal assistant, or to be placed in a special education classroom. A cost-offset analysis, from a payer's perspective (the local government responsible for school financing), was conducted comparing the costs of both interventions with the potential cost-savings due to a reduction in the prevalence of mental health problems and averted additional support required. The school district was comprised of 6,256 students, with 310 students receiving additional support for their mental health problems. Of these, 143 received support in their original school due to either having ADHD (n = 111), psychosocial problems (n = 26), or anxiety/depression (n = 6). The payers' total cost of additional support was 2,637,850 Euro per school year (18,447 Euro per student). The cost of running both interventions for the school district was 953,643 Euro for one year, while the potential savings for these interventions were estimated to be 627,150 Euro. The estimated effects showed that there would be a reduction of students needing additional support (25 for ADHD, eight for psychosocial problems, and one for anxiety/depression), and the payer would receive a return on their invested resources in less than two years (1.5 years) after implementation. Preventive school interventions can both improve some children's mental health problems and be financially beneficial for the payer. However, they are still limited in their scope of reducing all students' mental health statuses to below clinical cut-offs; therefore, the preventive school interventions should be used as a supplement, but not a replacement, to current practices. The findings have political and societal implications, in that payers can reallocate their funds toward preventive measures targeting students' mental health problems, while reducing the costs. When evaluating public health actions, it is necessary to consider their economic impact. The resources are scarce and the decision makers need knowledge on how to allocate their resources in an efficient way. Cost-offset analysis is seen as one way for decision makers to comprehend research findings; however, such analyses tend to not include the full benefits of the interventions, and actual impacts need to be fully evaluated in routine implementation

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J Psychiatr Res. 2016 Jun;77:67-75.

CHILDHOOD ADVERSITY AND PSYCHIATRIC DISORDER IN YOUNG ADULTHOOD: AN ANALYSIS OF 107,704 SWEDES.

Bjorkenstam E, Burstrom B, Vinnerljung B, et al.

Childhood adversity (CA) is associated with increased risks of psychiatric disorder in young adulthood, but details in this association are less known. We aimed to explore the association of a range of CA indicators with psychiatric disorder in young adulthood, and the impact of age at exposure, disorder type and accumulation of indicators. We capitalized on Sweden's extensive and high-quality registers and analyzed a cohort of all Swedes (N = 107,704) born in Stockholm County 1987-1991. Adversities included familial death, parental substance misuse and psychiatric disorder, parental criminality, parental separation, public assistance recipiency and residential instability. Age at exposure was categorized as: 0-6.9 years (infancy and early childhood), 7-11.9 years (middle childhood), and 12-14 years (early adolescence). Psychiatric disorders after age 15 were defined from ICD codes through registers. Risks were calculated as Hazard Ratios (HR) with 95% confidence intervals (CI). Results showed that exposure to at least one CA was associated with an increased risk of psychiatric disorder (HR 1.4, 95% CI: 1.3-1.4). Risks were increased for mood, anxiety, and psychotic disorders and ADHD but not for eating disorders. The risk varied with type of disorder but was similar for all exposure periods. Individuals with multiple (3+) CAs had a two-fold risk of psychiatric disorder (HR 2.0, 95% CI: 1.9-2.1). In conclusion, our findings support the long-term negative impact of CA on mental health, regardless of developmental period of exposure. Given that experience of CA is common, efforts should be put to alleviate the burden of childhood adversities for children, particularly among the most disadvantaged

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J Psychiatr Res. 2016 Jun;77:116-24.

SLUGGISH COGNITIVE TEMPO IN CHILDREN REFERRED TO A PEDIATRIC SLEEP DISORDERS CENTER: EXAMINING POSSIBLE OVERLAP WITH SLEEP PROBLEMS AND ASSOCIATIONS WITH IMPAIRMENT.

Becker SP, Garner AA, Byars KC.

Research supports the distinctness of sluggish cognitive tempo (SCT) (e.g., mental confusion and slowed behavior/thinking) from other psychopathologies. However, the relation between SCT and sleep functioning has not been adequately studied. We examined the association between SCT and sleep functioning in 325 children (62% male) ages 6-10 years referred to a pulmonary-based, accredited Sleep Disorders Center. Correlations between caregiver ratings of SCT, other psychopathologies (i.e., inattention/hyperactivity, oppositionality, depression, anxiety), sleep functioning (both behavioral and organic symptoms), as well as sleep disorder diagnoses, were examined. Unique effects of SCT and other psychopathologies on sleep problem severity controlling for child demographics were assessed using regressions. Regression analyses were also conducted to examine the unique effects of SCT on impairment (i.e., academic difficulties, parenting stress, and other psychopathologies) controlling for child demographics, sleep problem severity, and other psychopathology symptoms. SCT was weakly to moderately correlated with most measures of sleep (rs = .07-.39) and moderately to strongly correlated with measures of daytime sleepiness (rs = .33 and .53). In the regression analyses, SCT was uniquely associated with greater sleep functioning severity and impairment in academic functioning. SCT was also uniquely associated with higher levels of depression and inattention/hyperactivity, but not anxiety, and negatively associated with oppositionality. Finally, SCT symptoms were uniquely associated with greater parent-child dysfunctional interaction. Findings demonstrate that SCT is related to, but not redundant with, sleep problems and daytime sleepiness specifically. Further, SCT remained associated with several domains of functional impairment in sleep-disordered children after controlling for clinically-relevant variables, highlighting the potential value in assessing SCT symptoms in children with sleep problems

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J Trauma Dissociation. 2016;17:199-206.

COGNITIVE DEFICITS AND POSTTRAUMATIC STRESS DISORDER IN CHILDREN: A DIAGNOSTIC DILEMMA ILLUSTRATED THROUGH A CASE STUDY.

Malarbi S, Muscara F, Stargatt R.

Studies investigating the neuropsychological functioning of children who experience trauma have predominantly focused on maltreated populations. This article presents a case study that details the longitudinal outcome of a girl who experienced a motor vehicle accident at 5 years of age. It highlights the clinical relevance of research investigating the neuropsychological impact of single-incident trauma on children. It illustrates difficulties clinicians face in discriminating between the effects of developmental delay, traumatic brain injury, attention-deficit/hyperactivity disorder, trauma, and posttraumatic stress symptoms or posttraumatic stress disorder, especially in children with compensable injuries. The state of the current literature is discussed, and directions for future research are provided

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J Abnorm Psychol. 2017;126:225-36.

INTERPERSONAL CALLOUSNESS AND CO-OCCURRING ANXIETY: DEVELOPMENTAL VALIDITY OF AN ADOLESCENT TAXONOMY.

Meehan AJ, Maughan B, Cecil CAM, et al.

Growing evidence suggests heterogeneity within interpersonal-callous (IC) youth based on co-occurring anxiety. The developmental validity of this proposed taxonomy remains unclear however, as most previous research is cross-sectional and/or limited to adolescence. We aimed to identify low-anxiety (IC/ANX±) and high-anxiety (IC/ANX-) IC variants, and compare these groups on (a) early risk exposures, (b) psychiatric symptoms from midchildhood to early adolescence, and (c) school-based functioning. Using the Avon Longitudinal Study of Parents and Children (ALSPAC), a prospective epidemiological birth cohort, modelbased cluster analysis was performed on children with complete age-13 IC and anxiety scores (n = 6,791). Analysis of variance was used to compare resulting clusters on (a) prenatal and postnatal family adversity and maternal psychopathology, and harsh parenting; (b) developmental differences in attention-deficit/ hyperactivity disorder (ADHD), conduct disorder (CD), oppositional defiant disorder (ODD), emotional difficulties, and low pro-social behavior at 7, 10, and 13 years; and (c) teacher-reported discipline problems, along with standardized test performance. We identified a 4-cluster solution: "typical," "low," "IC/ANX±", and "IC/ANX-." IC/ANX- youth showed the highest prenatal and postnatal levels of family adversity and maternal psychopathology, highest levels of ADHD, CD, ODD, and emotional difficulties, greatest discipline problems, and lowest national test scores (all p<.001). IC/ANX-also showed a distinct pattern of increasing psychopathology from age 7 to 13 years. Adolescent IC subtypes were successfully validated in ALSPAC across multiple raters using prenatal and early postnatal risk, repeated measures of psychopathology, and school-based outcomes. Greater prenatal environmental risk among IC/ANX- youth suggests an important target for early intervention

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J Autism Dev Disord. 2017;1-12.

DO HANDWRITING DIFFICULTIES CORRELATE WITH CORE SYMPTOMOLOGY, MOTOR PROFICIENCY AND ATTENTIONAL BEHAVIOURS?

Grace N, Enticott PG, Johnson BP, et al.

Handwriting is commonly identified as an area of weakness in children with autism spectrum disorder (ASD), but precise deficits have not been fully characterised. Boys with ASD (n = 23) and matched controls (n = 20) aged 8–12 years completed a simple, digitised task to objectively assess handwriting performance using advanced descriptive measures. Moderate to large associations were identified between handwriting performance and attention, ASD symptoms and motor proficiency. The ASD group demonstrated significantly less smooth movements and significantly greater sizing variability and peak velocity relative to controls.

These findings provide a clearer indication of the specific nature of handwriting impairments in children with ASD, and suggest a relationship with core clinical symptom severity, attention and motor behaviours

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J Child Adolesc Psychopharmacol. 2016;26:828-34.

INFLUENCE OF AGE, GENDER, AND LIVING CIRCUMSTANCES ON PATTERNS OF ATTENTION-DEFICIT/HYPERACTIVITY DISORDER MEDICATION USE IN CHILDREN AND ADOLESCENTS WITH OR WITHOUT INTELLECTUAL DISABILITIES.

Osunsanmi S, Turk J.

Aims and Objectives: The aim of the study was to determine whether there are differences in psychopharmacological practice for attention-deficit/hyperactivity disorder (ADHD) in children and adolescents dependent on the presence or absence of associated intellectual disability; and if there are, whether the differences are influenced by factors such as age, gender, and living circumstances.

Methodology: A case-control cross-sectional design was used. Each arm of the study had a total of 107 children and adolescents aged 5-18 years. Case participants had diagnoses of having intellectual disability and ADHD; comparison participants had diagnoses of having ADHD, but no intellectual disability. Outcome measurements were (1) concurrent use of medications - single medication event as against concurrent multiple medication events - and (2) type of medication used - stimulants versus nonstimulants. Demographic factors considered were gender, age, and living circumstances.

Results: Male-to-female ratio in each group was 90:17. Mean age in the case group was 10.93 years (standard deviation [SD]: 3.39 years) and in the comparison group, 12.34 years (SD: 3.22 years). Seventy percent of the case group lived with their biological families, while 84% of the comparison group did so. In the case group, 7.5% were in residential school placements compared with only 0.9% of the comparison group. There were no statistically significant differences in broad measurements of outcomes between the case and comparison groups. Age appeared to be an important moderating factor for type of medication prescribed. Younger children with intellectual disabilities and ADHD were more likely to be established on nonstimulant medications than those with ADHD and no intellectual disabilities ($p = 0.024$, odds ratio: 1.8; 95% CI: 1.2-2.7).

Conclusions: Being between the ages of 5 and 12 years and having intellectual disability and ADHD are associated with raised likelihood of being prescribed nonstimulant medications for ADHD. This difference is maintained irrespective of gender and living circumstances. Reasons for these differences in prescribing practice require further exploration

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J Child Adolesc Psychopharmacol. 2016;26:798-806.

EFFECTS OF ATOMOXETINE IN INDIVIDUALS WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER AND LOW-FUNCTIONING AUTISM SPECTRUM DISORDER.

Kilincaslan A, Mutluer TD, Pasabeyoglu B, et al.

Objectives: This naturalistic, retrospective study investigated the effects of atomoxetine (ATX) on attention-deficit/hyperactivity disorder (ADHD) symptoms and autistic features in children with autism spectrum disorders (ASDs) and intellectual disability (ID).

Methods: Participants (n = 37, age range 6-17 years, mean: 10.16 ± 3.60) were assessed at baseline, 4th and 12th weeks using Clinical Global Impressions (CGI) scales, DSM-IV-based ADHD-rating scale (ADHD-RS), and amended Turkish version of Aberrant Behavior Checklist (ABC). The primary outcome measure was a treatment response defined by a CGI-improvement score of 1 or 2 together with a decrease of at least 25% in the parent-rated ADHD-RS total score at the end of 12th week.

Results: Five patients (13.5%) stopped medication at 4 weeks due to ineffectivity (2) and intolerable side effects (increased motor activity and talkativeness [n = 1], irritability [n = 2], temper outbursts [n = 2], and increased blood pressure [n = 1]). Sixteen patients (43.2%) were judged to be responders according to primary outcome measure. Improvement rate on CGI scale was 48.8%. On ADHD-RS, there were significant reductions between baseline and 4th week and between baseline and 12th week in both hyperactivity and inattention, and between baseline and 12th week in impulsivity scores. Decrease was significant in

hyperactivity and social withdrawal subscales of the parent-reported ABC. Responders based on primary outcome measure were not significantly different from nonresponders in terms of sociodemographic features or clinical parameters, including intellectual, language, autism symptom, and ADHD symptom levels.
Conclusion: In this chart review, ATX appears to be safe and effective for social withdrawal and ADHD symptoms in children with ASD and ID

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J Child Adolesc Psychopharmacol. 2016;26:860-61.
INCREASE IN MENSTRUAL CYCLE LENGTH INDUCED BY EXTENDED-RELEASE METHYLPHENIDATE IN AN ADOLESCENT WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.
Mutlu C, Bahall K, Gunes H, et al.

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J Child Adolesc Psychopharmacol. 2016;26:807-14.
CAREGIVER SATISFACTION WITH A MULTISITE TRIAL OF ATOMOXETINE AND PARENT TRAINING FOR ATTENTION-DEFICIT/HYPERACTIVITY DISORDER AND BEHAVIORAL NONCOMPLIANCE IN CHILDREN WITH AUTISM SPECTRUM DISORDER.
Hollway JA, Aman MG, Mendoza-Burcham MI, et al.
Objective: The purpose of this study was to examine caregiver satisfaction with the research experience in a randomized clinical trial of atomoxetine (ATX) and parent training (PT) for attention-deficit/hyperactivity disorder (ADHD) and behavioral noncompliance co-occurring with autism.
Methods: The Children with Hyperactivity and Autism Research Treatment Study (CHARTS) randomly assigned 128 children 5.00-14.11 years of age to four treatment groups (ATX + PT, ATX alone, PT + placebo[PBO], and PBO). Caregivers completed an 18 item questionnaire about their satisfaction with the research experience. We summarized caregiver responses with descriptive statistics and examined whether the responses were associated with demographic variables, treatment assignment, or the child's response to treatment (positive or negative).
Results: Ninety-three percent of caregivers (119) completed the questionnaire. When asked if they would join the study again if given the chance, 87% (103) responded "yes," 13% (15) responded "maybe," and 1% (1) responded "no." When asked if they would recommend the study to other caregivers of children with similar problems, 92% (109) responded "yes" and 8% responded (10) "maybe." Of the 59 Parent Satisfaction Questionnaire (PSQ) respondents who received PT, 75% (44) felt more confident in managing current child behaviors, 24% (14) felt that their level of confidence was unchanged, and 2% (1) felt less confident. Most caregivers expressed satisfaction with the study procedures, including the number of visits and the safety monitoring protocols.
Conclusions: In general, caregivers were highly satisfied with their research experience. These findings may be useful for informing human subject committees and for designing study protocols that are appealing to families

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J Commun Disord. 2016.
DISFLUENCY CHARACTERISTICS OF CHILDREN WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER SYMPTOMS .
Lee H, Sim H, Lee E, et al.
The purpose of the current study was to investigate the characteristics of speech disfluency in 15 children with attention-deficit/hyperactivity disorder (ADHD) symptoms and 15 age-matched control children. Reading, story retelling, and picture description tasks were used to elicit utterances from the participants. The findings indicated that children with ADHD symptoms produced significantly more stuttering-like disfluencies (SLD) and other disfluencies (OD) when compared to the control group during all three tasks. Further statistical analysis showed that children with ADHD symptoms produced more OD during the story retelling task than the other two tasks, whereas no significant differences in OD were observed among the

three tasks in the control children. Finally, children with ADHD symptoms exhibited a higher proportion of SLD in total disfluencies (TD) than the control children. These results are consistent with previous studies that children with ADHD are disfluent in their verbal production. Furthermore, children with ADHD symptoms seem to be more vulnerable to a speaking task that places greater demands on their attentional resources for language production, resulting in increased speech disfluencies

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J Indian Assoc Child Adolesc Ment Health. 2017;13:10-25.

EFFICACY OF A MODEL ATTENTION TRAINING PROGRAM FOR CHILDREN WITH ADHD.

Halder S, Mahato A.

Background: Attention Deficit Hyperactivity Disorder (ADHD) is one of the most common neurobehavioral disorders of childhood. Children with ADHD have problems with attention span and tend to be very easily distracted. They have difficulty in paying and maintaining attention over prolonged periods of time, along with difficulty in focusing and screening the stimulus presented in their surrounding environment. Effective intervention may improve their attention span over time, helping them to be more productive in school and at home.

Aim The present study aims to find out the efficacy of a 12-week attention training program for children with ADHD, aged 8-12 years, to improve attention of these children.

Method: Following purposive sampling, 15 children with ADHD were selected for attention training. Baseline assessment of inattention and hyperactivity symptoms of the subjects was done through parent reported rating scale. Attention training was delivered in individual session and included training module focussed on sustained, selective, alternative, and divided attention. Participants completed an outcome evaluation after 12 weeks of training program.

Results: Post training there was improvement in attention and reduction in scores of severity in attention scale.

Conclusion: Attention training for children with ADHD to improve attention span is effective and could be part of comprehensive management plan for children with ADHD

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J Paediatr Child Health. 2016;52:85.

EXECUTIVE FUNCTIONING AND ATTENTION IN EXTREMELY PRETERM CHILDREN ACROSS THREE ERAS.

Burnett AC, Cheong JLY, Carse E, et al.

Background: Extremely preterm/extremely low birth weight (EP/ELBW, <28 weeks/<1000 g) children have more difficulties with executive functioning (EF) and attention than term-born children. However, it is unknown how EF and attention outcomes have changed for EP/ELBW children over time.

Method: Three prospective geographical cohorts of EP/ELBW and control children (born in 1991-92, 1997, and 2005) were assessed at age 7-8 years. Parents rated everyday EF (behavioural regulation and metacognition) on the Behavior Rating Inventory of Executive Function. The 1997 and 2005 cohort parents also rated attention deficit hyperactivity disorder (ADHD) symptoms (Conners scales).

Results: Behavioural regulation difficulties did not vary by era, and were consistently greater in EP/ELBW children than controls (0.28 standard deviations [SD] above the control mean, p<.001). EP/ELBW children had more metacognition difficulties than controls (0.43 SD above control mean). This difference was greatest in the 2005 EP/ELBW cohort (0.65 SD above control mean, interaction p = .03). The 2005 EP/ ELBW group was also more likely to have elevated ADHD symptoms compared with the 1997 EP/ELBW group (interaction p = .04). This pattern persisted after covarying for maternal age, length of neonatal hospitalisation, family structure, and source of family income.

Conclusions: Contemporary EP/ELBW children continue to be at risk of EF and attention difficulties. Parents of EP/ELBW children born most recently identify even greater everyday EF problems and ADHD symptoms compared with earlier birth eras

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J Pediatr Urol. 2016.

IMPORTANCE OF NEUROPSYCHIATRIC EVALUATION IN CHILDREN WITH PRIMARY MONOSYMPTOMATIC ENURESIS.

Gulisano M, Domini C, Capelli M, et al.

Background: Nocturnal enuresis (NE) is an involuntary voiding during sleep. It is a very common disorder in school-age children. Comorbid psychopathologies are common in patients affected by enuresis. According to the ICCS, the rate of behavioral and emotional disorders in children with enuresis is doubled compared with healthy control (HC) children.

Objective: The aim of the present study was to investigate the prevalence of neuropsychiatric comorbidities in children affected by NE.

Study design: Two hundred children with a diagnosis of enuresis were recruited from the Neuropsychiatric Unit of Catania University and 200 age-matched neurologically intact HC children were recruited from local schools. The inclusion criteria were a normal IQ and the absence of other pathological clinical conditions such as diabetes or kidney malformation. The exclusion criteria were failure to complete the initial evaluation or clinical/diagnostic procedures, inability (because of young age) to complete study questionnaires, and severe neurological or physical impairment.

Results: Age and gender proportions were not significantly different between the groups. In the NE group, 138 subjects (69%) had a familial history of NE, compared with 24 subjects (12%) in the HC group ($p < 0.01$). The NE group demonstrated significantly higher scores in the Child Behavior Check List, Conners' Multidimensional Anxiety Scale for Children, and the Child Depression Inventory compared than the HC group as well as the Yale Global Tic Severity Score and Child-Yale-Brown Obsessive Compulsive Scale scores ($p < 0.01$). Quality of life scores were significantly lower in the NE group than in the HCs group; specifically, between-group differences were significant in the relationship and self domains ($p > 0.01$ for both comparisons) (Figure).

Discussion: The present case-control study evaluates the prevalence of different neuropsychiatric comorbidities in children with NE as diagnosed according to the new ICCS criteria. An important finding was that neuropsychiatric conditions were more prevalent in NE patients than in age-matched HC subjects. To the best of our knowledge, this is the first study to report associations between enuresis and obsessive compulsive disorder as well as tic disorder, and is the first to describe the comparative psychopathological profiles of 200 children with enuresis and 200 matched HC children.

Conclusion: The results suggest that clinicians should not underestimate the effects of enuresis on psychosocial development. Childhood NE should be managed carefully and comprehensively in order to prevent the development of more serious behavioral problems in the future. Display Omitted

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J Pediatr. 2016.

A CASE REPORT OF REVERSIBLE TAKOTSUBO CARDIOMYOPATHY AFTER AMPHETAMINE/ DEXTROAMPHETAMINE INGESTION IN A 15-YEAR-OLD ADOLESCENT GIRL.

Toce MS, Farias M, Bruccoleri R, et al.

Stimulant medications are used in the treatment of attention deficit hyperactivity disorder and serious cardiac complications can occur when these medications are abused. We present a 15-year-old adolescent girl who was found to have a Takotsubo cardiomyopathy after acute amphetamine/dextroamphetamine ingestion

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Journal of Psychotherapy Integration. 2017.

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. 2016;55:S272.

ADVANCES IN THE NEUROBIOLOGY OF ATTENTION-DEFICIT/HYPERACTIVITY DISORDER AND RELATED DISORDERS.

Biederman J, McGough JJ.

Objectives: The goal of this session is to advance knowledge on the neurobiology of ADHD and related disorders.

Methods: This group of studies relied on individual datasets to address the specific scientific issues examined.

Results: Dr. Stephen V. Faraone used data from the ADHD subgroup of the Psychiatric Genomics Consortium and the iPSYCH-SSI-Broad ADHD group to conduct a new analysis on the genetics of ADHD. The final sample size comprises 17,893 individuals with ADHD and 31,174 control subjects. Results showed several loci with genomewide significance and evidence for a significant polygenic background of common DNA variation and provided the first genomewide significant findings for biological mechanisms that have not been implicated in ADHD until now. Dr. Thomas J. Spencer examined the therapeutic potential of coadministering the mixed opioid antagonist naltrexone with methylphenidate (MPH) by conducting a 6-week double-blind, placebocontrolled RCT of naltrexone in adults with ADHD who received open treatment with therapeutic doses of MPH. The coadministration of naltrexone with MPH did not interfere with the clinical effectiveness of MPH for ADHD. Dr. Mai Uchida used resting-state fMRI to examine the neural basis of emotional dysregulation in a sample group of children at risk for major depression. Results showed that children at-risk manifest atypical functional connectivity in the default mode, cognitive control, and affective networks, which could represent biomarkers of risk for depression in the young. Dr. Amy Yule used familial risk analysis to re-examine the association between ADHD and SUDs, with attention given to proband sex. Results revealed that ADHD and SUDs in the proband were associated consistently with a significant risk for the same and opposite addictive (drug or alcohol) disorder in relatives independently of proband sex, indicating a common familial risk between ADHD and SUDs. Dr. Joseph Biederman's study assessed the implications of autism traits (ATs) in a large sample group of youth with ADHD of both sexes without a diagnosis of autism by relying on a unique profile of the Child Behavior Checklist to define ATs. Results showed that a substantial minority of children with ADHD manifests ATs, and those exhibiting them have greater severity of illness and dysfunction.

Conclusions: This group of studies provides new insights into the neurobiology and pharmacology of ADHD and related disorders

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J Am Acad Child Adolesc Psychiatry. 2016;55:S226.

RELATIONSHIP BETWEEN ENVIRONMENTAL LEAD EXPOSURE AND NEUROCOGNITIVE PERFORMANCE IN ATTENTION-DEFICIT/ HYPERACTIVITY DISORDER WITH EVIDENCE OF NORADRENERGIC GENE-LEAD INTERACTION.

Choi JW, Jung AH, Kim KM, et al.

Objectives: We aimed to evaluate specific neurocognitive functions that are associated with blood lead levels and investigate associations of those functions with interactions between lead and dopaminergic and noradrenergic genotypes in youth with ADHD.

Methods: Two hundred sixty-seven youth with ADHD and 101 healthy controls (aged 5 to 18 years) participated in this study. A semi-structured interview (K-SADS-PL) was conducted with each participant of both groups for psychiatric diagnostic evaluation. Blood lead levels were measured0 noradrenergic genotypes for ADHD, namely dopamine transporter (DAT1), dopamine receptor D4 (DRD4), and alpha-2A-adrenergic receptor (ADRA2A) genotypes were investigated. All participants were assessed using the ADHD Rating Scale-IV (ADHD-RS), and they also completed the continuous performance test (CPT) and the Stroop color-word test (SCWT). ANCOVA was used for comparison of the blood lead levels between ADHD and control groups. Multivariable linear regression model was used to evaluate associations of blood lead levels with the results of ADHD-RS, CPT, and SCWT; IQ, age, and gender were adjusted. Path analysis model was used to identify mediating effects of neurocognitive functions between blood lead levels and ADHD symptoms.

Results: There was a significant difference in blood lead levels between the ADHD and control groups (1.4±0.5 vs. 1.3±0.5 ++g/dL, p=0.004). Blood lead levels showed a positive correlation with scores on omission errors of CPT (r=0.16, p=0.01) and on hyperactivity-impulsivity subscale of ADHD-RS (r=0.14, p=0.03). In the multivariable linear regression model, blood lead levels were associated with CPT omission errors (B=0.14, p=0.02). Regarding effects of lead on ADHD symptoms, hyperactivity-impulsivity were mediated by omission errors of CPT. An interaction effect was detected between ADRA2A genotype and lead level on omission errors (B=0.12, p=0.04).

Conclusions: Our results showed that blood lead levels are associated with ADHD symptoms, with a mediating effect of neurocognitive functions and the neurocognitive functions are affected by the interaction between blood lead levels and noradrenergic genotype

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J Am Acad Child Adolesc Psychiatry. 2016;55:S215.

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

Bilgi A, Toker A, Isik U, et al.

Objectives: Neurobiological, pharmacological, and molecular genetic studies support the role of neurotrophic factors in ADHD. Among neurotrophic factors, brain-derived neurotrophic factor (BDNF) is the most investigated one, but recent studies have pointed out the possible role of other neurotrophic factors such as glial-derived neurotrophic factor (GDNF) and neurotrophin-3 (NT3) for the etiopathogenesis of this complex disorder. Nerve growth factor (NGF) may also be related to ADHD, but no previous studies have investigated the potential role of NGF in ADHD. In the present study, we explored the serum levels of BDNF, GDNF, NT3, and NGF in children with ADHD.

Methods: The sample consisted of 110 drug-naive children with ADHD combined subtype ages 7-18 years and 44 healthy controls. Depression and anxiety symptom levels of the participants were evaluated by self - report inventories. Plasma levels of neurotrophins were measured using commercial enzyme-linked immunosorbent assay (ELISA) kits. Multivariate analyses of covariance (MANCOVAs), with age, gender, and anxiety and depression levels as covariates, were used to examine the differences among the groups in serum levels of neurotrophins.

Results: Multivariate effects of ADHD and control groups were significant for the serum neurotrophin levels (Pillai's trace=0.07; F=2.58 df=3,145, p=0.040 +Àp2=0.066). Pairwise comparisons with Bonferroni correction showed that the mean serum NT3 and GDNF levels were significantly higher in children with ADHD than in the control subjects (F=4.53 df=1,145, p=0.035, +Àp2=0.030 and F=4.79 df=1,145, p=0.030, +Àp2=0.031 respectively). However, serum BDNF and NGF levels did not differ between groups.

Conclusions: The results of this study suggests increased serum NT3 and GDNF levels in untreated children with ADHD. However, our findings indicate no alteration of serum BDNF and NGF levels in these children

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J Am Acad Child Adolesc Psychiatry. 2016;55:S218.

DEFICITS IN ANATOMICAL AND FUNCTIONAL CONNECTIVITY IN MEDICATION NAIVE CHILDREN WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.

Choi J, Yoo J, Teicher MH, et al.

Objectives: Alterations of ADHD subjects extend into widespread brain structures, which were presented by different imaging modalities. This study investigates anatomical and functional connectivity feature sets that can distinguish medication-naïve children with ADHD from typically developing children (TDC).

Methods: Neuroimaging features included 66 functional connectivities (FC) among 12 resting-state functional networks, diffusion metrics in 20 fiber tracts as anatomical connectivity (AC), and 33 structural features. Single or any kind of combination of FC, AC, or structural features with demographic information were entered in a multiple support vector machine recursive feature elimination algorithm (https://github.com/johncolby/SVM-RFE) to select optimal feature sets for prediction of the diagnostic status of individuals with 19 ADHD from 20 age-, sex-matched TDC. Both out-of-bag error (OOB) as mean prediction error and area under the curve in each set were able to get the results from random forests, which returned the predicted label with the probabilities of all possible outcomes. The final winner set was validated with an independent multimodal dataset (27 ADHD and 13 TDC).

Results: The final winner set included both FCs, such as a left central executive network (CEN), with a right CEN or with salience network and ACs such as the axial diffusivity of hippocampal portion of the left cingulum bundle. This winner set had better performance than AC only ($Z = -3.295$, $P < 0.001$) and then FC only ($Z = -2.091$, $P = 0.037$) and explained 18.05 percent of the variation of the ADHD rating scale. We were able to identify medication-naïve ADHD from TDC with 7.69 percent of OOB. This winner set also showed superior performance than both tensor ($Z=-2.071$, $P = 0.038$) and marginal significance to FC only by a bootstrap method ($D = 1.890$, $P = 0.059$, 5000 replicates) in an independent validation dataset.

Conclusions: Our results with multivariate approaches indicate aberrant anatomical and functional brain circuitry that could explain the multiple symptom domains in ADHD. Our results from small sample group sizes having overfitting tendency should be treated with care and be confirmed with large datasets

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J Am Acad Child Adolesc Psychiatry. 2016;55:S166-S167.

STEPPED TREATMENT FOR ATTENTIONDEFICIT/ HYPERACTIVITY DISORDER AND AGGRESSIVE BEHAVIOR: A RANDOMIZED TRIAL OF RISPERIDONE, VALPROATE, AND PLACEBO AFTER OPTIMIZED STIMULANT MONOTHERAPY.

Blader JC, Pliszka SR, Kafantaris V.

Objectives: This study evaluated a stepped treatment for youth aged 6-12 years with ADHD, a disruptive behavior disorder, and aggressive behavior. Children first completed open stimulant monotherapy titrated to an optimal regimen. If aggression persisted, they proceeded to a randomized trial comparing risperidone (RISP), divalproex sodium (DVPX), and placebo (PBO) adjunctive to stimulant treatment.

Methods: Eligibility criteria included ADHD, ODD/CD, and prior treatment with a stimulant (30 mg per day methylphenidate or equivalent), surpassing thresholds on standardized behavior-rating scales. Treatment began with a protocol to establish optimal stimulant dosage and concurrent family-based behavioral therapy. Length of this phase varied to accommodate individual differences in regimens attempted [mean = 62 days (SD = 33)]. Aggression nonremitters were allocated to RISP, DVPX, or PBO in a 2:2:1 ratio for an 8- week trial. Primary outcome was changed in parent-rated aggressive behavior on the Retrospective-Modified Overt Aggression Scale (R-MOAS). Secondary outcome had changed in the Aggressive Behavior scale of the Child Behavior Checklist (CBCL-Agg).

Results: A total of 175 children began the trial. Among the 151 children completing open stimulant monotherapy, 96 (64 percent) experienced remission of aggressive behavior and were not randomized. Among those receiving blinded adjunctive treatment, RISP and DVPX groups showed greater reductions

compared with PBO in R-MOAS ratings [adjusted mean standardized differences (MSD), -1.26 and -0.86, respectively] and CBCLAgg scores (MSD, -1.14 and -0.83, respectively). Weight gain was significantly greater in the RISP group.
Conclusions: The high rate of robust outcomes of stimulant monotherapy was unexpected for this highly impaired cohort (94 percent in special education, 18 percent with prior psychiatric emergency department or inpatient admission, 24 percent receiving prior antipsychotic treatment, all with insufficient stimulant response in community care). This finding suggests that rigorous optimization of first-line stimulant monotherapy should be exhausted before initiating cotherapy, potentially reducing use of antipsychotic agents in this patient population. For those with stimulant-refractory aggression, risperidone has a large effect size, whereas DVPX has a smaller effect size, but weight gain with RISP treatment remains a significant concern

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J Am Acad Child Adolesc Psychiatry. 2016;55:S264.

SEQUENCING TREATMENTS FOR MOTHERS WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER AND THEIR YOUNG CHILDREN: A SMART PILOT.

Chronis-Tuscano A.

Objectives: Young children of mothers with adult ADHD are at risk for ADHD by virtue of genetics and environmental factors. Moreover, parent ADHD is associated with maladaptive parenting and poor child behavioral treatment response. Thus, a combined approach consisting of behavioral parent training (BPT) and maternal stimulant medication (MSM) may be needed to effectively treat ADHD within families. However, providing combined BPT+MSM initially to all families may be unnecessarily burdensome given that not all families need combined treatment. The ultimate purpose of this study is to examine how to combine, sequence, and personalize treatment for these multiplex families to yield benefits to both the parent and child, thereby affecting the course of child ADHD and disruptive behavior symptoms and thus reducing the need to medicate young children, in line with the guidelines of the American Academy of Pediatrics.
Methods: In this presentation, we will describe our rationale behind the study, its design, and preliminary results (based on N = 26 participants) with an ongoing pilot Sequential Multiple Assessment Randomized Trial (SMART) designed to answer these questions.
Results: Preliminary results on observational parenting outcomes will be highlighted.
Conclusions: We also will discuss how the subsequent full-scale SMART might change based on what is learned in the SMART pilot and illustrate how the full-scale SMART could be used to inform clinical decision-making on combining, sequencing, and personalizing treatment for young children and families in which a parent has ADHD

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J Am Acad Child Adolesc Psychiatry. 2016;55:S145.

SPECIFIC DIFFERENCES IN AUDITORY BRAIN STEM RESPONSE IN YOUNG PATIENTS WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.

Claesdotter-Hybbinette EL, Cervin M, +àkerlund S, et al.

Objectives: The auditory brainstem response (ABR) is often affected in neurodevelopmental disorders. The aim of this study was to investigate differences in ABR in young females and young males with ADHD compared to control subjects.
Methods: We studied 63 drug naïve females with ADHD and no comorbidity (mean 13.8 years, SD 2.5), 26 female controls with no psychiatric record (mean 13.8 years, SD 2.7), 48 drug naïve males with ADHD and no comorbidity (mean 13.1 years, SD 1.8), and 20 male controls with no psychiatric record (mean 12.8 years, SD 1.7). All patients were diagnosed according to the DSM-IV. The ABR consists of seven peaks (wave I-VII) that occur 10 ms following a stimulus recorded by electrodes on the mastoid processes of each ear and on the forehead.
Results: Comparing the ABR of 63 girls with ADHD to 26 age correlated control subjects 3 traits were identified, denoted TR6, TR14 and TR15. The higher value in TR6 (p=0.000064), is explained by more aberrant curve profiles in the thalamic region. In TR14, the aberration was found in a region from superior

olivary complex to thalamus (p=0.00059). TR15 (p=0.00035), is explained by more aberrant curve profiles in the lateral leminiscus. When looking at the ABR from 48 young males with ADHD and comparing them to 20 age correlated control subjects, we found 3 traits; TR4, TR5 and TR14. TR 4 is a lower correlation to a norm curve in inferior colliculus and thalamic area (p=0.00105). TR5 identifies irregular curve profiles representing the nucleus cochlea (p=0,00027). TR14, is described as an aberration in superior olivary complex to thalamus(p=0.00013). Bonferroni correction was used to account for multiple comparisons.
Conclusions: These data indicate specific aberrations in the ABR in ADHD subjects compared to normal controls. Young females with ADHD exhibited a significantly different ABR in a region between cochlear nucleus and superior olivary complex and in the thalamic region. In the male ADHD group ABR aberrancy was found in the midbrain region and in the more peripheral part; nucleus cocleus. To further substantiate our findings there is a need for longitudinal studies with control subjects with other psychiatric diagnoses

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J Am Acad Child Adolesc Psychiatry. 2016;55:S223-S224.
DEMOGRAPHICS OF CHILDREN WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER AND TREATMENT MODALITIES: AN ANALYSIS OF NATIONAL AMBULATORY MEDICAL CARE SURVEY DATA FROM 2009-2012.
Dietzold J, Garg A, Peters I, et al.
Objectives: Wide variation in ADHD diagnostic and treatment practices exists across providers in the US for children. This study describes the demographics of children with ADHD, and examines what factors influenced treatment.
Methods: The National Ambulatory Medical Care Survey (NAMCS) is a comprehensive survey performed yearly on outpatient US visits. For this study, NAMCS data from 2009 to 2012 was used. Participants were included if they were between the ages of 5 and 18 and carried a diagnosis of ADHD (ICD9 codes 314.00/314.01). Treatment was considered as receiving a stimulant, psychotherapy/mental health counselling, or both. Data was analyzed in SAS 9.1 by chi-squared tests.
Results: From 2009 to 2012 there were 53,051,522 outpatient encounters involving children with ADHD. Of those visits, 65 percent were male, 87 percent were white, 59.9 percent were between the ages of 13-18, and most had either private insurance (54.1 percent) or Medicaid/Children's Health Insurance Program (CHIP) (26.7 percent). About 36.6 percent had a comorbid psychiatric diagnosis. The most common treatment modality was stimulants only (55.8 percent), followed by stimulants and therapy (21.3 percent) and then therapy only (6.4 percent). There was a group of children who received no treatment at all (16.5 percent). Of the patients who were diagnosed with ADHD, those who had comorbid psychiatric diagnosis were more likely to receive any treatment (38.0% vs 29.4%, p<0.03), as were those in the 13-18 years-old range (61.2% vs 53.1%, p<0.02). However, among those diagnosed with ADHD, race and insurance were not associated with receiving treatment.
Conclusions: This study supports the previously identified trend demonstrating age disparities in treating ADHD in children. Also, the high percentage of children in this sample who were white (87 percent) compared to the percentage of white children in the US population overall (51.6 percent) suggests racial disparities in diagnosing ADHD. Once identified with ADHD, there was no evidence of race impacting the receipt of treatment. This suggests barriers to accessing care. Future research should focus on identifying the sources of these barriers in order to design interventions to reduce racial and age inequalities

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J Am Acad Child Adolesc Psychiatry. 2016;55:S330.
EFFICACY AND COST-EFFECTIVENESS OF INDIVIDUAL VERSUS GROUP-BASED PARENT TRAINING FOR PRESCHOOL ATTENTION-DEFICIT/ HYPERACTIVITY DISORDER: A MULTI-CENTER RANDOMIZED CONTROLLED TRIAL.
Daley D.
Objectives: The goal of this presentation is to compare the efficacy and cost effectiveness of New Forest Parenting Programme (NFPP)-an individually delivered approach-with a group-based approach (incredible years, IY) and treatment as usual (TAU) in a sample group of preschool children with ADHD.

Methods: The Comparison of Preschool Parenting Interventions (COPPI) trial was a three-arm parallel group, randomized controlled trial. The trial recruited 307 preschool children that met standard ADHD diagnostic criteria. Children were block-randomized to NFPP, IY, or TAU on a 3:3:1 ratio. NFPP is a specialist parent-training (PT) program for parents of preschool children with ADHD delivered on a one-to-one basis. The toddler version of IY is a group-based PT program delivered over 12-weekly sessions designed to address problems of challenging and oppositional conduct in young children.
Results: In total, 307 participants were randomized (NFPP: N = 134; IY: N = 131; TAU: N = 42). The sample group included a high proportion of single parents (30 percent), low-income families, children with language difficulties (50 percent), and parents with mental health problems (77 percent). No statistically significant differences between NFPP and IY were observed in parent-assessed ADHD symptoms at T2 (primary end point: mean for NFPP, 1.715; mean for IY, 1.724; mean difference, -0.009; 95% CI -0.191 to 0.173; p = 0.921) or T3 or in other secondary or healthrelated outcomes at either T2 or T3. Small benefits of NFPP over TAU were seen for parent-rated ADHD (adjusted mean, 1.693 for NFPP and 1.881 for TAU; mean difference, -0.189; 95% CI -0.380 to 0.003; p = 0.053) and conduct problems (p < 0.05). NFPP was significantly less costly than IY (mean total cost per patient, -ú1,509 vs. -ú2,103), with the difference being attributed to higher intervention-related costs of IY. Cost utility analysis, in terms of incremental cost/quality-adjusted life-year (QALY) gained, showed that NFPP was dominant over IY and thus likely to be cost-effective, albeit based on small QALY gain differences.
Conclusions: High-quality, group-based PT may be more expensive to deliver than some forms of individually delivered equally efficacious PT programs. Both formats should be available to families

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EPIDEMIOLOGY OF ATTENTION-DEFICIT/ HYPERACTIVITY DISORDER AND SUBSTANCE USE DISORDERS: DEFINING A HIGH-RISK GROUP.

Denman M.

Objectives: ADHD and SUD have high prevalence among children and adolescents and confer significant harm to well-being. Overlap between the two disorders not only would suggest a subgroup for indicated prevention, but also might suggest that treatment strategies for preexisting ADHD could affect the future risk of SUD. Furthermore, there may be mediating and moderating variables that affect the onset of SUD in ADHD, which also could be important targets for intervention.
Methods: We will review longitudinal twin studies, family studies, and other epidemiological studies to report the overlap of ADHD and SUD and review alternate measures of risk in children.
Results: ADHD is a risk-factor for SUD, even when factoring out CD. The presence or absence of CD may simply reflect a behavioral inhibition dimensional trait that varies across individuals with ADHD. CD shares some of the same environmental risks as early onset SUD. Moving beyond the categorical diagnoses, a dimensional approach to ADHD shows that, symptom by symptom, there are increases in substance use risk for those with inattentive ADHD criteria. In addition, hyperactive-impulsive symptoms confer risk independently. An empirical symptom-based approach, the transmissible liability index, demonstrates that there are symptoms that reliably increase the risk of SUD cutting across domains, including sleep, appetite variability, skin-picking, conduct symptoms, oppositional symptoms, inattention, and hyperactive/impulsive symptoms. Although the construct of risk taking might be important, it is an amalgam of at least two different domains, approach and avoidance. A previous study demonstrated an ADHD subtype labeled as surgent, featuring excessive behavioral approach-possibly an excellent endophenotype to study for future SUD risk. A final question of comorbidity is a variant of the self-medication hypothesis. ADHD individuals cite symptom relief as a reason for use; however, longitudinal data do not support the idea that efficacious symptom reduction is a main driver of increased use.
Conclusions: Understanding the overlap between SUD and ADHD helps clinicians prepare for potential risks through judicious clinical management. ADHD individuals are a useful target for indicated measures of prevention

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J Am Acad Child Adolesc Psychiatry. 2016;55:S323.

ADULT FUNCTIONAL OUTCOMES AND THEIR PREDICTORS IN INDIVIDUALS WITH CHILDHOOD ATTENTION-DEFICIT/HYPERACTIVITY DISORDER: RESULTS FROM THE LONG-TERM FOLLOW-UP OF THE MULTIMODAL TREATMENT STUDY OF ATTENTION-DEFICIT/HYPERACTIVITY DISORDER (MTA).

Hechtman L, Roy A.

Objectives: The goals of this session are as follows: 1) to describe adult functional outcomes in individuals with childhood ADHD followed prospectively for 16 years in the Multimodal Treatment Study of Attention-Deficit/ Hyperactivity Disorder (MTA); and 2) determine baseline factors that influence these functional outcomes.

Methods: Data were collected at baseline and in young adulthood (ages 12, 14, and 16 years after baseline; mean age = 25 years) for 453 participants with a childhood diagnosis of ADHD (MTA group) and 241 healthy age- and sex-matched classmates (LNCG, or Local Normative Comparison Group). The MTA group was subdivided in continuation (persisters) versus remission (desisters) of ADHD symptoms. All participants were assessed for the following baseline factors: IQ, childhood comorbidities, parent-child relationships, parent mental health problems, parental marital problems, parenting practices, household income levels, and parental education. Functioning outcomes in young adulthood were obtained for domains of education, occupation, legal involvement, emotional functioning, substance use, and sexual behavior.

Results: Three patterns of functional outcomes emerged. First, LNCG fared best, persisters did worst, and desisters fared in between for outcomes of the following: obtaining a bachelor's degree, times fired/quit a job, current income, receiving public assistance, emotional lability, and risky sexual behavior. Second, for emotional outcomes and marijuana and any substance use disorder, LNCG and desisters did not differ and fared better than persisters. Third, with nicotine and alcohol use disorders, jail time, and the number of jobs held, the three groups showed no significant differences. In the MTA group, baseline IQ predicted adulthood income levels and likelihood of obtaining a bachelor's degree. A high parental education was associated with obtaining a bachelor's degree, and parental marital problems were associated with an increase in risky sexual behavior. Childhood comorbidities were associated with emotional lability problems in both MTA and LNCG groups.

Conclusions: Functioning outcomes vary among adults with a childhood ADHD and are influenced by different childhood factors depending on outcome domains. Therefore, treatment must be ongoing and comprehensive, addressing ADHD and comorbidities, to improve adult functioning outcomes

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J Am Acad Child Adolesc Psychiatry. 2016;55:S323.

PREDICTORS OF ADULT OUTCOME IN ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.

Hechtman L, Rohde LA.

Objectives: The objective of this session is to identify key predictors of adult outcome in individuals with childhood ADHD.

Methods: Four large studies of children with ADHD and matched control subjects who were followed prospectively into adolescence and adulthood will be presented, with an emphasis on factors that may predict adult outcome. Studies will include the New York Study, headed by Dr. Rachel Klein; the Pittsburgh Study, headed by Drs. Bill Pelham and Brooke Molina; the Berkeley Girls Study, headed by Drs. Stephen Hinshaw and Elizabeth Owens; and the seven-site Multimodal Treatment Study of ADHD. The adult age of participants in these studies ranges from 20 to 41 years. Various predictors of adult outcome are explored.

Results: Persistence and severity of ADHD and comorbidity, particularly conduct disorder/antisocial personality disorder, which often leads to SUD and criminality, were important predictors. Depression, and its contribution to self-injurious behavior and suicidality, was also identified as an important predictor, particularly in girls. Parenting, IQ, SES, and social impairment also have an impact on some outcome domains.

Conclusions: Adult outcome in ADHD is not uniform. It falls into three groups as follows: 1) those with fairly normal outcome; 2) those with significant symptoms of the syndrome and impaired functioning in academic, occupational, social, and emotional domains (w50 percent); and 3) a small subgroup (10-20 percent) with significant negative outcome-poor education, marked unemployment, significant alcohol/substance use

disorder, and important psychiatric and antisocial symptoms. Persistence of ADHD and comorbid CD and antisocial personality disorder are important predictors for this last outcome group. Treatment needs to address ADHD, its comorbidities, and impairment in an ongoing way for this chronic lifelong condition

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J Am Acad Child Adolesc Psychiatry. 2016;55:S128.

A COMPARISON OF BRAIN NETWORKS BETWEEN ATTENTION-DEFICIT/HYPERACTIVITY DISORDER AND BIPOLAR DISORDER IN MEDICATION-NAÏVE ADOLESCENTS: A PRELIMINARY RESTING-STATE FMRI STUDY.

Han DH, Park J, Hyun GJ, et al.

Objectives: ADHD and BD are frequently comorbid in adolescents and have several symptoms in common. Few studies compared the brain networks between medication-naïve adolescent BD and ADHD. The goal of the current study was to examine whether brain networks can aid in the differentiation between BD and ADHD.

Methods: The study participants were medication-naïve male adolescents (aged 13-18 years), who met the DSM-5 criteria for BD (N = 16) or ADHD (N = 15), and age-matched healthy male adolescents (N = 15). All participants completed the ADHD Rating Scale (ADHD-RS) and Young Mania Rating Scale (YMRS). By use of a 3.0 Tesla MRI scanner, we assessed resting-state functional connectivity (RSFC) within five networks as follows: the affective network, ventral attention network, dorsal attention network, cognitive control network, and default mode network. To correct for multiple comparisons in the cluster analysis, the resulting maps were set to a threshold of $P < 0.01$, with a family-wise corrected type I error.

Results: Compared with ADHD, BD showed greater RSFC within the ventral attention network from the left inferior frontal gyrus to the left middle frontal gyrus ($P = 0.001$). They also showed decreased RSFC within the dorsal attention network from the right frontal eye field (FEF) to the left middle frontal gyrus ($P = 0.009$) and from the right FEF to the right precuneus ($P = 0.007$), within the cognitive control network from the left dorsolateral prefrontal cortex (DLPFC) to right superior frontal gyrus ($P = 0.002$) and from the right DLPFC to the right superior frontal gyrus ($P = 0.004$), and within the default mode network from the left precuneus to the right precuneus ($P = 0.002$) and the right cingulate gyrus ($P = 0.008$) and from the right precuneus to the left precuneus ($P = 0.009$). In adolescents with BD, YMRS scores were correlated negatively with the RSFC in the affective network between the left anterior cingulate cortex and the left hippocampus ($r = -0.70$, $P = 0.003$).

Conclusions: Compared with ADHD, BD showed greater RSFC within ventral attention networks and decreased RSFC within the dorsal attention, cognitive control, and default mode networks

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J Am Acad Child Adolesc Psychiatry. 2016;55:S226.

GLUTAMATERGIC NETWORK GENE MUTATIONS IN ADOLESCENTS AND CHILDREN WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.

Elia J, Khan M, Kim C, et al.

Objectives: This study aimed to estimate the prevalence of rare, recurring copy number variants (CNVs) of specific metabotropic glutamate receptor (GRM, mGluR) and related network genes in a pediatric population with ADHD.

Methods: A multicenter, noninterventional genotyping study was conducted in children/adolescents with ADHD diagnosis, based on multiple lines of evidence of glutamatergic involvement in ADHD pathogenesis, including significant association between ADHD occurrence and disruptions (CNVs) in GRM gene family and interacting genes (Elia J et al. Nature Gen 2012; 44:78- 84). 2-mL saliva samples (Oragene-Dx) were submitted to The Children's Hospital of Philadelphia genotyping laboratory. Analysis used OMNI-2.5M genotyping assay for CNVs of 79 previously identified GRM and directly related genes significantly enriched in ADHD vs. non-ADHD controls (Tier 1 genes) and CNVs in nearly 200 other glutamatergic network genes (Tier 2 genes).

Results: Of 918 subjects with ADHD enrolled by 23 sites, genotype data were available from 892 subjects (children, age 6 to <12 years: n=269; adolescents, age 12 to 17 years: n=623). A total of 200 subjects had

mutations in glutamatergic network genes (overall prevalence, 22.4 percent), of which 138 (69 percent) were Tier 1 mutations and 62 (31percent) were Tier 2 mutations. The distribution of mutations in children (n=71, 26 percent) was 56 (79 percent) Tier 1 and 15 (21 percent) Tier 2 mutations; distribution in 129 (21 percent) mutation-positive adolescents was 82 (64 percent) Tier 1 and 47 (36 percent) Tier 2 mutations.
Conclusions: In this clinical US population of children/adolescents with ADHD, the 22.4 percent observed prevalence of glutamatergic network mutations approximated hypothesized rate of 20-25 percent. Based on these findings, a substantial proportion of ADHD population may be candidates for mGluR-directed therapy

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EARLY ENVIRONMENTAL EXPOSURES AS SHARED AND UNIQUE RISK FACTORS IN CHILDHOOD MENTAL ILLNESS: RESULTS FROM LARGE-SCALE EPIDEMIOLOGICAL STUDIES.
Grice DE, Hudziak JJ.
Objectives: This symposium focuses on the identification and understanding of familial and environmental exposures on childhood mental health.
Methods: Association between childhood maltreatment and inflammation in control subjects and individuals with affective disorders was measured in New Zealand and UK cohorts. Data on women and their daughters from Avon Longitudinal Study of Parents and Children on maternal pre-pregnancy BMI, daughter BMI, and pubertal development were analyzed, as were data on eating disorders (EDs). In Finnish national registers, perinatal data were examined as risk factors for ADHD. In a Danish national cohort, associations of risk for ASD, ADHD, OCD, and TD/chronic tic (CT) and parental age were studied. Systematic review and meta-analyses of environmental risk factors for ASD were performed.
Results: Maltreated children had elevated inflammation levels as adults, levels that, in turn, were associated with depression. Maternal overweight in pre-pregnancy was associated with higher levels of offspring ED behaviors, whereas maternal underweight predicted lower levels. The risk effect of maternal overweight was mediated by childhood growth between ages 7 and 13 years, but the protective effect of maternal underweight was more complex. Declining Apgar scores increased ADHD risk, as did elective cesarean section, maternal high blood pressure, nulliparity, breech presentation, induction of labor, and treatment in a neonatal intensive care unit. Advancing parental age was associated increased risk for ASD, whereas younger maternal or paternal age was associated with increased ADHD risk. Younger maternal age increased risk for ASD and TD/CT; advancing paternal age increased risk of ADHD. Several environmental factors (vaccination, maternal smoking, air pollution, thimerosal, and reproductive treatments) are unlikely to be related to risk of ASD. Birth complications show strong links to ASD.
Conclusions: Parental age, maternal health, obstetric factors, perinatal complications, childhood trauma, and other early environmental exposures can relate to phenotypic risk and clinical outcomes. Some factors appear to increase risk differentially according to phenotype or disorder, whereas other factors cross diagnostic boundaries

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J Am Acad Child Adolesc Psychiatry. 2016;55:S225.
AN INITIAL INVESTIGATION OF BRAIN FUNCTIONAL REORGANIZATION FOLLOWING ORGANIZATIONAL SKILLS TRAINING IN CHILDREN WITH ATTENTION-DEFICIT/ HYPERACTIVITY DISORDER.
Chen B, Somandepalli K, Abikoff HB, et al.
Objectives: Organizational Skills Training (OST), is a 10-week psychosocial intervention found effective in improving organizational, time management, and planning (OTMP) skills in children with Attention-Deficit/Hyperactivity Disorder (ADHD). Little is known about the feasibility of identifying brain markers for treatment response. Using resting state fMRI (R-fMRI), we aimed to examine neuronal correlates of post-treatment change as a first step toward larger controlled studies of objective predictors of treatment response.
Methods: We examined pre- and post-OST R-fMRI data of 15 children (12 males; mean age: 9±1 year) with ADHD and significant impairments in OTMP skills indexed by total scores on Children's Organizational Skills Scales-Parent (COSS-P) or Teacher (COSS-T). Our primary outcome measure was the change in COSS-P

scores. As secondary summary outcome measure, we used prepost Z-score differences averaged across COSS-T, Homework Problems Checklist, Academic Progress Report and Academic Performance Rating scales. We selected a priori the intrinsic functional connectivity (iFC) of the dorsal anterior cingulate cortex (dACC), based on its role on cognitive control. Multivariate distance matrix regression (MDMR) analysis additionally allowed for whole-brain explorations. Follow-up iFC analyses were conducted on regions with significant within-subject post-OST differences by MDMR analysis.
Results: COSS-P decreased significantly (t=7.1, p< 0.0001). In a cluster involving striatum bilaterally, dACC iFC decreased post-OST; these decreases were positively correlated with COSS-P improvements (r=.34, NS) and to improvements in the summary outcome (r=.63; p<0.03). MDMR analyses revealed iFC changes in the right medial and lateral precentral cortex. Followup seed-based iFC analyses of this region showed significant decreases in cortico-striatal iFC post-OST.
Conclusions: Results support the feasibility of identifying changes in brain iFC after OST. Two distinct analysis converged on decreased corticosubcortical iFC post-treatment which related to change in clinical measures. As decreases in striato-cortical iFC characterize typical development, results suggest regionally-specific enhanced maturational effects of OST

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J Am Acad Child Adolesc Psychiatry. 2016;55:S101.

FACIAL AFFECT RECOGNITION IN AUTISM SPECTRUM DISORDER, ATTENTION-DEFICIT/ HYPERACTIVITY DISORDER, AND TYPICAL DEVELOPMENT.

Berggren S, Engstrom AC, B+Âlte S.

Objectives: ASD and ADHD have been associated with explicit facial affect recognition (FAR) alterations, but comparative studies are scarce. This study examined FAR accuracy and response times for overall and specific basic emotions FAR performance in whole-face and eye-region stimuli.
Methods: FAR was assessed in matched sample groups of children and adolescents with ASD (n = 35), ADHD (n =32), and typical development (TD) (n = 32) aged 8.6-15.9 years (mean age = 11.6 years; SD = 2.0).
Results: Compared with TD, the group with ASD showed less accuracy and longer response times for general and specific FAR, mostly driven by problems in neutral and happy face identification. The group with ADHD responded faster than the group with ASD for global FAR. No differences between ADHD and TD were found. Attentional distractibility had a significant effect on FAR performance in ASD and ADHD.
Conclusions: Findings confirm FAR alterations in ASD, but not ADHD, and endorse effects of attentional distractibility on FAR in ASD and ADHD. FAR and attention function training is clinically meaningful in ASD, as well as additional attention training in ASD and ADHD to improve FAR. Future studies should include control for visual attention and facial configuration skills, use naturalistic FAR material, and also investigate implicit FAR

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J Am Acad Child Adolesc Psychiatry. 2016;55:S227.

MATERNAL AND PATERNAL PSYCHOPATHOLOGY EFFECTS ON THE SOCIAL FUNCTIONING OF CHILDREN WITH DISRUPTIVE BEHAVIOR PROBLEMS.

Babinski DE, Waschbusch DA, Andrade BF, et al.

Objectives: Many parents of children with disruptive behavior problems experience substantial stress and psychopathology. While numerous studies have documented parental psychopathology effects on parent and child functioning in the home setting, very little is known about how parental psychopathology impacts childhood outcomes beyond the home setting. This study examines associations between parental psychopathology and peer functioning in the school setting among children with disruptive behavior problems.
Methods: Participants were 104 mothers and 76 fathers of children (mean age=9.61 years old) attending a therapeutic summer day camp. Most children were boys (74.3 percent) and met diagnosis for ADHD and/or comorbid ODD/CD (78.9 percent). Parents completed self-report assessments of depression, anxiety, anger,

ADHD, and conduct problems, and teachers completed ratings of children's peer functioning. Parenting behaviors, including positive involvement, negative/ineffective discipline, and deficient monitoring, were also examined as moderators of relations between parental psychopathology and peer functioning.
Results: Maternal depression, ADHD, anxiety, and anger were all associated with greater teacher-rated peer problems (r=0.23-0.29; p<.05). Maternal positive involvement moderated relations between maternal depression and anger and peer functioning, such that higher levels of involvement were associated with better peer functioning. Paternal depression and anger were related to child peer problems (r=0.23-0.28; p<.05), but statistically significant effects were not found regarding paternal anger, ADHD, conduct problems, or anxiety. Paternal behavior did not moderate these associations.
Conclusions: These results suggest that the effects of parental psychopathology extend beyond the home setting and are important considerations in children's social functioning. School-based treatments that address family functioning may serve to optimize social emotional outcomes for children with disruptive behavior disorders

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PREDICTIVE VALUE OF GLUTAMATERGIC NETWORK GENE MUTATION TESTING FOR ATTENTION-DEFICIT/HYPERACTIVITY DISORDER IN CHILDREN AND ADOLESCENTS IN AN OUTPATIENT PSYCHIATRY SETTING.

Hakonarson H, Kao C, Squires LA, et al.

Objectives: This study aimed to estimate the predictive value of rare, recurring copy number variants (CNVs) of specific metabotropic glutamate receptor (GRM, mGluR) and related network genes for ADHD in an outpatient pediatric psychiatry population.
Methods: Recently, a large-scale, genome-wide study comparing copy number variations (CNVs) in 3,500 ADHD cases vs. 13,000 controls revealed that rare, recurring CNVs impacting specific glutamate receptor metabotropic (GRM) genes (i.e., GRM1, GRM5, GRM7, and GRM8) occurred in ADHD patients at significantly higher frequencies compared with healthy controls (Elia et al. Nat Genet, 2012). The Children's Hospital of Philadelphia (CHOP) Center for Applied Genomics (CAG) biorepository includes genotyped samples from over 80,000 patients and first-degree relatives seen at CHOP. A search of the CAG repository identified 3,445 subjects previously seen at CHOP psychiatry clinic who had been genotyped on the 550HH or 610Q SNP arrays from Illumina and evaluated for mGluR mutations as previously described.
Results: Of 155 subjects with GRM network CNVs, 138 subjects had been diagnosed with ADHD according to electronic medical records (EMRs). Of the 17 subjects without EMR diagnosis of ADHD, parents of 14 subjects were contacted by phone. Of these, parents of 12 subjects reported that their children had been diagnosed with ADHD; 1 had been diagnosed with Down's Syndrome; 1 subject had no history of ADHD.
Conclusions: In this population of children/adolescents identified as having mGluR network mutations of interest, 97% were identified as having ADHD based upon EMR review and/or parent interview. These results suggest that rare recurrent CNVs in mGluR network genes may play an important role in the pathobiology underlying ADHD

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THINKING OUTSIDE THE PILL BOX: INITIAL RESULTS OF A RANDOMIZED CONTROLLED TRIAL OF A NOVEL PLAY-BASED INTERVENTION FOR PRESCHOOL ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.

Halperin J.

Objectives: Training Executive, Attention, and Motor Skills (TEAMS) is a playbased intervention designed to facilitate neurodevelopment and improve the clinical trajectories of preschool children with ADHD. An open clinical trial indicated clinical improvement that persisted 3 months after treatment as indicated by parent and teacher ratings. This initial double-blind RCT was conducted to estimate effect sizes of TEAMS relative to an active comparison intervention so that parameters for a larger, more adequately powered, RCT could be determined.

Methods: Preschool children (N = 53) with ADHD were randomized to 5 weeks of treatment with TEAMS (n = 27) or a closely matched control intervention (n = 26). Clinical and neuropsychological assessments were conducted by separate evaluators who were blind to the treatment group at four time points: pretreatment, posttreatment, 1-month follow-up, and 3- month follow-up.
Results: Two-way (group +ù time) mixed-model ANOVAs yielded several significant main effects for time, indicating clinical and neuropsychological improvements after treatment. However, there were few significant main effects or interactions involving group. Separate examinations of effect size for TEAMS and the comparison condition relative to pretreatment at all three posttreatment time points indicated consistently larger effect sizes for TEAMS as judged by parents (1.24, 0.72, 0.96 vs. 0.38, 0.65, 0.55, respectively), teachers (0.96, 0.85, 0.57 vs. 0.56, 0.74, 0.30, respectively), and clinicians (0.84, 0.97, 0.57 vs. 0.54, 0.52, 0.43, respectively). Yet, between- group effect sizes were small. Within the active treatment group, time engaged in TEAMS activities was associated with better clinical outcomes.
Conclusions: Findings show some promise for TEAMS, but further development is warranted. Ways to modify the intervention to improve efficacy will be discussed

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J Am Acad Child Adolesc Psychiatry. 2016;55:S282.

A GENOME-WIDE ASSOCIATION STUDY OF A COGNITIVE ENDOPHENOTYPE OF ATTENTION-DEFICIT/ HYPERACTIVITY DISORDER IN A COMMUNITY-BASED PEDIATRIC SAMPLE .

Crosbie J.

Objectives: The power of genome-wide association studies (GWAS) of ADHD is reduced by clinical/genetic heterogeneity and insufficient clinical sample group sizes. Use of a cognitive endophenotype for ADHD, such as response inhibition, could decrease heterogeneity and increase power. Novel methods such as the hypothesis-driven GWAS (GWAS-HD) could also help identify possible biological pathways involved in response inhibition [e.g., central nervous system (CNS) development]. The GWAS-HD conducts genome-wide hypothesis testing while prioritizing single nucleotide polymorphisms (SNPs) within genes involved in the hypothesized pathway. We conducted a GWASHD to test the role of SNPs involved in CNS development on response inhibition measured in a large community pediatric sample group. Methods: Salivary DNA and performance on a measure of response inhibition [stop-signal reaction time (SSRT) from the stop-signal task] were collected on 17,263 youth (age 6-17 years) visiting a science museum. We genotyped 5,366 unrelated Caucasians using Illumina HumanCoreExome bead chips and analyzed 4,970 sample groups at 9,598,793 imputed and genotyped SNPs. For the GWAS-HD, individual SNPs in the CNS development set were tested using stratified false discovery rate, whereas the whole geneset was tested using permutation tests for association with SSRT.
Results: Ninety-four percent of the sample group passed quality control (N = 4,687). Several SNPs approached genome-wide significance ($p = 1.3 \times 10^{-7}$). The set of CNS development SNPs were associated significantly with SSRT.
Conclusions: SNPs that alter CNS development may be involved in response inhibition and potentially ADHD (yet to be tested). Measurement of cognitive endophenotype such as response inhibition in a large community sample group is a feasible and potentially powerful alternative strategy for psychiatric genetics

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J Am Acad Child Adolesc Psychiatry. 2016;55:S337.

NATIONAL TRENDS IN ATTENTION-DEFICIT/ HYPERACTIVITY DISORDER CARE.

Hoagwood K, Crystal S, Bilder S, et al.

Objectives: Closing the gap between evidence-based clinical practices and routine care for children with ADHD is an important public health goal.
Methods: Medicaid enrollment, claims, and prescription drug disbursement data from the Medicaid Analytic Extract (MAX) from 20 states for 2001 to 2010 were analyzed for children with ADHD (ages 3-17 years). Treatment services were analyzed to compare rates of medication, psychotherapy, and combined treatment services.

Results: The proportion of children of low income who were diagnosed with ADHD rose by 83 percent. Rates of comorbidity were high (43.3 percent in 2010), an increase of 13 percent over the study period. There was a 74 percent increase in combined treatment; psychotherapy alone increased by 52 percent, and rates of medication alone decreased by 18 percent.
Conclusions: More children received treatments that appeared to conform to clinical practice standards over the decade

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J Am Acad Child Adolesc Psychiatry. 2016;55:S51.

DETERMINING NEUROFEEDBACK-SPECIFIC EFFECT IN ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.

Arnold LE.

Objectives: The goal of this session is to determine whether neurofeedback (NF) has a specific benefit for ADHD. Nonblinded RCTs have shown encouraging results, but small blinded, flawed RCTs have not. Giving 30 to 40 sessions of attention and coaching, with electrodes connected, is likely to yield much placebo and other nonspecific benefits. Literature reflects disagreement about the specific effect of NF. Despite wide variation in the quality of NF, it has the potential to be an alternative or adjunct tomedication, with amore enduring effect.
Methods: A pilot study demonstrated that blinding is possible, families are willing to enter a trial-risking sham treatment, retention is >85 percent, and families prefer treatment three times per week over twice per week. However, the treatment in that pilot study was not optimal, lacking important coaching and using fuzzy logic rather than manually set thresholds. A combination of NF experts, mainstream ADHD experts, RCT experts, a design/ statistical expert, and a technical software expert teleconferenced weekly for over a year to design a study with optimal downward training of theta-beta ratio (TBR) and double blinding.
Results: A method of double blinding was implemented; deartifacted prerecorded EEGs from patients of the same age, who were receiving clinical NF of the same type used in the study, were played for sham participants with their real-time muscle artifacts superimposed. Neither the patient nor the NF trainer could tell whether the screen EEG was from the patient or a sham group. It was programmed remotely by an off-site coinvestigator. We originally planned for four sites with 180 participants; however, the NIMH budget cap required us to reduce the number of participants to 140 (84 active, 56 sham) at two sites. Age range was 7-10 years because at approximately age 11 years, there is a natural reduction of TBR that would complicate assessment. A TBR of >4.5 was required. Established stimulant medication was allowed but was required to be cleared from the system 5 to 7 days before major assessments. Treatment course was 38 sessions, with sessions 20 and 40 reserved for major assessments. Children who did not begin to improve by session 20 were required to exit from the study and enter other treatment programs.
Conclusions: The double-blind RCT of NF was in its second day of 5 years. To date, 105 have been screened (50 randomized); 74 percent of children ages 7-10 years with ADHD (77 percent of boys, 63 percent of girls) had a TBR >4.5. Vitamin D insufficiency was found in 29 percent, four times as many in Columbus, Ohio and in Asheville, North Carolina

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J Am Acad Child Adolesc Psychiatry. 2016;55:S124.

THE EFFECT OF GRIN2B AND DRD4 POLYMORPHISMS ON LOCAL FUNCTIONAL CONNECTIVITY IN ATTENTION-DEFICIT/ HYPERACTIVITY DISORDER.

Kim JI, Yoo J, Jeong B, et al.

Objectives: Genetics studies have identified significant relationships between ADHD and N-methyl-D-aspartate (NMDA) receptor genes. However, phenotypical correlates of brain functions associated with these genes have yet to be investigated. We examined the association of GRIN2B, an NMDA receptor-related gene, and the dopamine receptor D4 (DRD4) gene exon III variable number tandem repeats 2-repeat allele with local functional connectivity in subjects with ADHD and control subjects.
Methods: A total of 67 ADHD subjects and 44 control subjects (aged 6-17 years) were recruited from a child and adolescent psychiatric clinic and completed genetic analyses and resting-state fMRI scans. The effects

of diagnosis, genotype, and the diagnosis-genotype interaction of the two genetic polymorphisms on the local resting-state functional connectivity using static regional homogeneity (ReHo) and its temporal characteristics, such as dynamic mean and SD, were examined by surface-based analysis. The correlation between the variables of the ReHo analyses showing significant diagnosis-genotype interaction and neuropsychological test scores were examined.
Results: There were significant diagnosis (P < 0.001) and interaction (P = 0.02) effects of GRIN2B on static ReHo in the left superior parietal cluster, and the ReHo value was correlated positively with the Children's Color Trails Test interference scores in the ADHD with T allele subgroup (P = 0.012). There also were significant diagnosis (P < 0.001) and interaction (P = 0.03) effects of the DRD4 gene on the dynamic ReHo SD in the right superior parietal cluster.
Conclusions: These results suggest that alterations in neurotransmission mediated by glutamate-dopamine interaction in ADHD may contribute to abnormalities in local functional connectivity and its dynamic repertoire

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J Am Acad Child Adolesc Psychiatry. 2016;55:S196.

LONG-TERM EFFICACY AND SAFETY OF EXTENDED-RELEASE MOLINDONE (SPN-810) TO MANAGE IMPULSIVE AGGRESSION IN CHILDREN WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.

Adewole T, Brittain ST, Johnson JA, et al.

Objectives: This study sought to assess overall clinical response during longterm use (up to 6 months) of extended-release molindone (SPN-810), a D2/ D5 antagonist, to manage impulsive aggression (IA) in children 6-12 yrs old with ADHD treated with optimized stimulant monotherapy.
Methods: Patients completing double-blind (DB), placebo-controlled doseranging study were eligible for open-label extension (OLE) in which SPN-810 dosages were adjusted according to clinical response after blinded conversion to 18 mg (<30 kg) or 36 mg (ΓëÑ30 kg). For DB study, patients had to have ADHD diagnosis and Retrospective-Modified Overt Aggression Scale (RMOAS) score 24 at screening and ΓëÑ20 after 3-wk OL stimulant optimization period. Key endpoints of interest: change in R-MOAS score and adverse event (AE) occurrence.
Results: Of 78 patients entering OLE, 52 (67 percent) completed it. Most common reasons for discontinuation: consent withdrawn (11.5 percent), AEs (9 percent), lost to follow-up (6 percent), investigator decision (4%). Median R-MOAS changes from DB baseline (from OLE baseline) were -31.5 (0), -25.0 (10), and -27.0 (0) at OLE maintenance doses of 18, 27, and 36 mg/day, respectively. Most common AEs considered possibly/definitely related to study medication: sedation (11.5 percent), increased appetite (9 percent), weight gain (8 percent), somnolence (5 percent). Total treatment-related AEs were dose related (9 mg/day, 13 percent; 36 mg/day, 33 percent). Two patients developed symptoms suggestive of EPS (dyskinesia, n=1; dystonia, n=1), which resolved with dose reduction (n=1) or with no action taken (n=1). Treatment-related AEs resulting in discontinuation (n=5): aggression (n=2), weight gain (n=2), tachycardia (n=1). No notable or systematic effects on laboratory assessments, vital signs, or ECGs.
Conclusions: Improvements in IA behavior achieved with SPN-810 treatment (R-MOAS change from DB baseline) were sustained during OLE treatment (stable R-MOAS score from OLE baseline). SPN-810 was generally well tolerated; AEs were consistent with types of events expected in children receiving low-dose SPN-810 added to ADHD medication

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J Am Acad Child Adolesc Psychiatry. 2016;55:S223.

SUBGROUPS IDENTIFICATION OF ATTENTION-DEFICIT/HYPERACTIVITY DISORDER IN DIMENSIONS OF SYMPTOM SEVERITY AND INTELLIGENCE USING TOPOLOGICAL DATA ANALYSIS AND THEIR FUNCTIONAL NETWORK MODULAR ORGANIZATIONS.

Kim E, Song J, Kyeong S, et al.

Objectives: ADHD is a clinically heterogenous condition, with deficits in multiple neuropsychological processes and related brain systems. The identification of subgroups with distinct patterns of clinical manifestation may lead to development of better-targeted intervention for individualized treatment. The two

main objectives of this study were to: 1) to identify distinct clinical phenotypes based on a symptom severity and intelligence quotient (IQ) of children and adolescents with ADHD; and 2) to investigate whether neuroimaging findings validates identified phenotypes.
Methods: Using resting state fMRI data from the ADHD-200 Consortium, 90 Typically developing controls (TDCs) and 114 children with ADHD from the NYU dataset and 100 TDCs and 71 children with ADHD from the PKU dataset was included in this study. Parent-rated ADHD symptom ratings and IQ were used as input features in topological data analysis (TDA) to identify subgroups within the sample. External validators including resting- state functional connectivity and network segregation and integration measures were reported for each subgroups of the ADHD sample to address the biological meaningfulness of the identified subtypes.
Results: The TDA suggested three subgroups: One TDC and two ADHD, labeled as mild ADHD (m ADHD) and severe ADHD (s ADHD) groups. The brain networks of each group demonstrated that sADHD subgroup showed decreased functional integration and increased functional segregation compared with both mADHD and controls. In the analysis of functional network modular organization, the s ADHD group displayed increased intramodule connectivity within the default mode network (DMN), visual network (VN), basal ganglia network (BGN) and a decreased inter-module connectivity between the DMN and VN, and an increased inter-module functional connectivity density (FCD)s between the salience network (SN) and temporal network (TN), and between the executive control network (ECN) and BGN, relative to TDC and m ADHD group.
Conclusions: We demonstrated that the use of common clinical phenotypes (symptom severity and IQ) and TDA is an informative approach for understanding the heterogeneity in ADHD. Also, whole-brain intrinsic functional connectivity showed that our classification of m ADHD and s ADHD group may be neurobiologically valid

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J Am Acad Child Adolesc Psychiatry. 2016;55:S142-S143.

SYMPTOMS RELATED TO PRENATAL EXPOSURE OF ALCOHOL AND SUBSTANCES MASQUERADING AS ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.

Herrera N, Griffin M.

Objectives: ADHD is a disorder marked by a consistent pattern of inattention and/or hyperactivity-impulsivity that interferes with functioning. It is one of the most prevalent mental health diagnoses identified in school-age children, increasing their risk for academic/social difficulties and psychiatric comorbidities. Often times, children with a history of prenatal exposure to alcohol and substances present to psychiatric clinics with symptoms of ADHD. Throughout my 12-week clinical experience in an urban outpatient university-based ADHD clinic, two such patients were evaluated.
Methods: First, we examine the case of a female patient (age 8 years) who presented with a history of premature delivery, failure to thrive, developmental delays, and in utero exposure to alcohol for evaluation of learning and behavioral concerns. Next, we will discuss the case of a male patient (age 9 years), with a past medical history of partial complex epilepsy (febrile seizures) and in utero exposure to cocaine and methamphetamine, who presented to the clinic for disruptive behavior and concerns of ADHD or ODD.
Results: Prenatal exposure to alcohol and substances are some of the most important preventable causes of birth defects, intellectual disability, and neurodevelopmental disorders. Heavy prenatal exposure to alcohol could lead to fetal alcohol spectrum disorders (FASD), which may include a variety of disorders composed of varying levels of physical, neurological, behavioral, and cognitive impairments. Prenatal cocaine exposure has been correlated with negative effects on behavior problems, alterations in various aspects of executive functioning, including visual-motor ability, attention, and working memory. Prenatal amphetamine exposure has negative effects on fetal growth and neurobehavior.

Conclusions: It is imperative to distinguish ADHD from similar symptoms caused by FASD and substance use because their treatment regimens will differ from those typically used to treat ADHD. A comprehensive literature search on ADHD and comorbid teratogen exposures will be conducted detailing the neuropathology of toxic exposures as related to the development of ADHD, as well as the diagnostic considerations when there is comorbidity

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J Am Acad Child Adolesc Psychiatry. 2016;55:S268-S269.

PERSISTENCE, REMISSION, AND EMERGENCE OF ATTENTION-DEFICIT/HYPERACTIVITY DISORDER IN YOUNG ADULTHOOD: RESULTS FROM A LONGITUDINAL, PROSPECTIVE, POPULATION-BASED COHORT.

Arseneault L.

Objectives: ADHD is now recognized as a disorder that occurs in adulthood. However, less is known about the prospective course of ADHD into adulthood, the risk factors for its persistence past childhood, and the possibility of its emergence in young adulthood in nonclinical populations. The aim of this study was to investigate childhood risk factors and young adult functioning of individuals with persistent, remitted, and lateonset ADHD.

Methods: The study sample group is the Environmental Risk (E-Risk) Longitudinal Twin Study, a birth cohort of 2,232 twins born in England and Wales from 1994 to 1995. ADHD diagnoses were assessed in childhood at ages 5, 7, 10, and 12 years and in young adulthood at age 18 years.

Results: The results showed that, among the individuals with childhood ADHD, 21.1 percent met criteria for ADHD at age 18 years. Persistence was associated with higher levels of symptoms and lower IQ in childhood. At age 18 years, persistent individuals had increased functional impairment and higher rates of other mental health problems compared to those who remitted. Among individuals with adult ADHD, 67.5 percent did not meet criteria for ADHD at any childhood assessment. In childhood, individuals with late-onset ADHD showed fewer behavior problems and higher IQ compared to the persistent group; at age 18, they exhibited comparable ADHD symptoms and impairment, as well as similarly elevated rates of mental health problems.

Conclusions: The findings indicate that persistence of ADHD is driven by childhood ADHD severity and neuropsychological impairment. Furthermore, we identified heterogeneity in the adult ADHD population, which may call into question the conceptualization of adult ADHD as a childhood-onset neurodevelopmental disorder

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J Am Acad Child Adolesc Psychiatry. 2016;55:S164.

DASOTRALINE PHARMACOKINETICS IN PEDIATRIC SUBJECTS WITH ATTENTION-DEFICIT/ HYPERACTIVITY DISORDER.

Hopkins SC, Sunkaraneni S, Sarma K, et al.

Objectives: Dasotraline is a dopamine and norepinephrine reuptake inhibitor with slow absorption and long elimination. Here, we report dasotraline single-dose pharmacokinetics (PK) in children and adolescents.

Methods: Male and female subjects (ages 6-17 years) with a diagnosis of ADHD were assigned to a series of sequential, escalating, single-dose dasotraline cohorts of 1, 2, 4, 8, 12, and 16 mg. Plasma samples were collected during a 2-day inpatient stay, followed by five daily outpatient visits (7 days postdose), and a follow-up visit at 14 days postdose. Dasotraline concentrations were measured by LC-MS/MS, and dasotraline PK were compared with those observed in adults by population modeling.

Results: All 105 enrolled subjects (50 children, 55 adolescents) contributed to the PK assessments; 72.4 percent were male. Single doses of dasotraline resulted in geometric mean Cmax values (±CV) ranging from 0.53 (±30 percent) to11ng/ml(±35percent) in children ages6-12yearsold, and0.34(±13percent) to 6.2 ng/ml (±23 percent) in adolescents ages 13-17 years. At every dose level, Cmax values were greater in the younger age cohorts, consistent with an approximately 60 percent greater body weight in the older subjects. Dasotraline was slowly absorbed with median tmax values between 9.6 and 12 hours across dose cohorts. Elimination was slow withmedian half-life values between 56 and 84 hours. No subjects discontinued because of an adverse event (AE). Across all ages and doses, 41.9 percent of subjects had an AE; the most common AE was tachycardia, observed in 23.8 percent of participants following dasotraline dosing and

predominantly characterized as mild; all other AEs occurred in less than 5 percent of subjects. Individual observed dasotraline concentrations in pediatric subjects fell within the predicted and prespecified range using a previously developed dasotraline population PK model based on adult subjects.
Conclusions: The results of this single-dose study found dasotraline to have a PK profile in pediatric subjects (ages 6-17 years) that is similar to adults, with slow absorption and a long elimination half-life. Clinical trial simulations indicated that dasotraline (2-4 mg/day) in children would yield exposures that are equivalent to adult subjects treated with 4-8 mg/day

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J Am Acad Child Adolesc Psychiatry. 2016;55:S222.

A META-ANALYSIS OF POTENTIALLY MODIFIABLE RISK FACTORS FOR CHILDHOOD ATTENTION-DEFICIT/ HYPERACTIVITY DISORDER: CHEMICAL EXPOSURES AND FACTORS RELATED TO PARENTING.

Holbrook JR, Claussen AH, Bitsko RH, et al.

Objectives: Both the physical and socioemotional environment impact child development, and risk factors in each of these categories may increase risk of ADHD. As part of a larger ADHD risk factor meta-analysis project, this paper reports on meta-analyses conducted to examine the potential impact of 1) early exposure to specific chemicals and 2) parenting factors on the later development of ADHD or ADHD symptoms.
Methods: A review of the chemical exposure literature and parenting literature respectively identified 51 and 26 studies with sufficient information to include in the analyses. Individual risk factors that were evaluated in three or more studies were analyzed.

Chemical exposures included: Brominated flame retardants (BFRs), which can be present in household items, such as upholstery, carpet padding, and mattresses; Lead (may be present in paint in older homes); Chemicals potentially ingested through the diet, including cadmium, polychlorinated biphenyls (PCBs), and hexachlorobenzene; and Organophosphates, a common group of pesticides.

Parenting factors included: Parenting quality (sensitivity/warmth, intrusion/reactivity, and negative/harsh discipline); and Maltreatment (general maltreatment and physical abuse).

Results: Childhood lead exposure was the most heavily studied chemical exposure, and it was consistently strongly associated with ADHD symptoms. Other statistically significant chemical exposures were organophosphates, PCBs, and BFRs. All of the parenting factors showed a significant association with ADHD, with the exception of physical abuse and negative/harsh discipline.
Conclusions: Numerous chemical exposures and parenting factors were found through this meta-analysis to be associated with modest, increased risk of ADHD. Findings support the continued need for primary prevention and targeted screening for childhood exposure to lead and other chemicals as potential avenues to prevent or reduce ADHD symptomatology among children. In addition, supporting positive parenting may represent an opportunity to improve ADHD symptoms

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J Am Acad Child Adolesc Psychiatry. 2016;55:S170.

PIVOTAL PHASE 3 TRIAL EVALUATING THE EFFICACY AND SAFETY OF HLD200, A NOVEL DELAYED-RELEASE AND EXTENDED-RELEASE FORMULATION OF METHYLPHENIDATE, IN CHILDREN WITH ATTENTION-DEFICIT/ HYPERACTIVITY DISORDER.

Arnold VK, DeSousa NJ, Incledon B, et al.

Objectives: Evening-dosed HLD200 delays the initial release of methylphenidate (MPH) by approximately 8-10 hours, targeting the onset of clinically meaningful treatment effect upon awakening and lasting to the evening. The objective was to determine whether HLD200 improves control of ADHD symptoms and at-home early morning and evening functioning versus placebo (PLA) in children with ADHD. Safety and tolerability were also assessed.
Methods: This was a pivotal, randomized, double-blind, multicenter, PLA controlled, parallel-group, phase 3 trial of HLD200 in children (age 6-12 years) with ADHD (Clinical Trial: NCT02520388). Subjects had current or prior response on MPH. After a screening period of Γëñ 2 weeks with a 3- to 7-day washout, subjects were randomized (1:1) to HLD200 or PLA once daily each evening for 3 weeks. After 1 week, the initial 40-mg

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

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J Am Acad Child Adolesc Psychiatry. 2016;55:S323-S324.

ADULT FUNCTIONAL AND PSYCHIATRIC OUTCOMES AMONG WOMEN WITH CHILDHOOD ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.

Ahmad S, Hinshaw SP, Owens E.

Objectives: Longitudinal studies of males with ADHD reveal information about long-term prognosis and predictors of adult outcome. We present adult outcomes from a large study of women diagnosed with childhood ADHD and test predictors, including childhood diagnostic status, comorbidity, and ADHD persistence.
Methods: Girls (N = 140, age 6-12 years) with ADHD (97 with combined and 43 with inattentive presentation; 88 comparisons) were recruited from community sources. Diagnostic status and comorbidities were determined using the Diagnostic Interview Schedule for Children-IV. Sixteen years later (mean age 25.6 years), outcomes included internalizing and externalizing problems (Adult Self-Report and Adult Behavior Checklist); parent, self, and clinician ratings of educational, occupational, and interpersonal impairment (Longitudinal Interval Follow-up Evaluation-Range of Impaired Functioning Tool); clinician assessment of substance use problems; and self-reported years of education, weekly hours worked, income, public assistance, and arrest/incarceration. We covaried child IQ, age, and socioeconomic status.
Results: ADHD versus comparison differences were significant for externalizing and internalizing problems (mean d = 0.71) and all measures of impairment (mean d = 0.78). Girls with childhood ADHD had significantly fewer years of education (d = 0.89), lower incomes (d = 0.57), and more arrest/incarceration (odds ratio = 3.4) than comparisons. Girls with childhood ADHD used more nicotine than comparisons (d = 0.48), but no other substance use differences were significant. There were no significant differences by presentation, with the exception that predominantly inattentive girls showed the most nicotine use and greater likelihood of arrest/incarceration. Across comorbidity groups, outcomes were statistically equivalent, with the exception of arrest/incarceration (non-comorbid girls showed the highest rate). Girls with persistent ADHD typically demonstrated worse outcomes than those with transient ADHD (mean d = 0.55), with the exception of years of education, income, and self-rated impairment.
Conclusions: Girls with childhood ADHD show poor adult outcomes in most domains, generally unrelated to childhood subtype or comorbidities. Whereas persistent ADHD is most deleterious, key outcomes (years of education, income, and self-ratings of impairment) suggest that childhood ADHD has pernicious, long-term effects

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J Am Acad Child Adolesc Psychiatry. 2016;55:S170-S171.

A PILOT, OPEN TRIAL OF BEHAVIORAL PARENT TRAINING VS. ROUTINE CLINICAL CARE AMONG PARENTS OF CHILDREN WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.

Ishii-Takahashi A, Kawakubo Y, Nakajima N, et al.

Objectives: We investigated the effect of behavioral parent training (BPT) on children's behavior and sensitivity to punishment and reward. The BPT focused on the parent providing a structured environment for the child, setting rules, giving clear instructions and rewarding appropriate behavior.

Methods: This open, pilot trial recruited mothers of children with attention deficit hyperactivity disorder (ADHD). They received 10 weeks of BPT + Routine Clinical Care (RCC) (n = 22) or 10 weeks of RCC (n = 13) alone. Outcomes were changed in parent-reported total behavior problem score, internalizing and externalizing problems scores measured by Child Behavior Checklist (CBCL), ADHD symptoms assessed by the ADHD Rating Scale IV, the child's reward processing style measured by the Sensitivity to Punishment and Sensitivity to Reward Questionnaire-Children (SPSRQ-C), parental stress (from the Parental Stress Index I), and Parental Perception Index (PPI-P: PPI-P positive and PPI-P negative).

Results: Using repeated measures ANOVA, we found BPT + RCC was more effective then RCC alone in reducing both externalizing and internalizing behavioral problems (CBCL, internalizing score: P = .02, externalizing score: P = .03) negative parenting (PPI-P negative: P = .001) and parenting stress (PSI total: P = .02). No treatment group differences were found for reduction in ADHD symptoms (ADHD-RS total: P = .73). At baseline, lower maternal ADHD symptoms (b = .653, P =.002) and higher responsiveness to social approval in children (b = -.513, P=0.001) were related to a more robust response to BPT.

Conclusions: BPT was superior to standard clinical care in improving a child's overall problems with behavior and reduced parental stress but had no impact on a child's core ADHD symptoms. As higher responsiveness to social approval in children predicted greater improvement the subgroup of children with ADHD and higher responsiveness to social approval may benefit most from the intervention. To test this hypothesis, we plan a randomized clinical trial, stratifying on the basis of social responsivity. Clinical trial registration information URL:https://umin.ac.jp/

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J Am Acad Child Adolesc Psychiatry. 2016;55:S142.

FAMILIAL TRANSMISSION OF ATTENTIONDEFICIT/HYPERACTIVITY DISORDER: A PILOT STUDY OF FATHERS WITH ATTENTION-DEFICIT/ HYPERACTIVITY DISORDER AND THEIR YOUNG CHILDREN.

Joseph HM, Perlman SB, Gnagy EM, et al.

Objectives: This study explores the association between paternal parenting behavior and ADHD in preschool-aged offspring of fathers with and without childhood histories of ADHD.

Methods: Participants of the Pittsburgh ADHD Longitudinal Study (PALS), with children between the ages of 3 and 7 years, were screened. Fathers completed the questionnaire on their parenting behaviors, child demographics, and the child's behavior and temperament. A semistructured psychiatric interview (Kiddie-Schedule for Affective Disorders and Schizophrenia) was completed with a clinician. The father and offspring pair performed a parent-child interaction task in the laboratory.

Results: The prevalence of ADHD is greater in off spring of fathers with childhood ADHD compared with control subjects (50 vs.10percent). Fathers with childhood ADHD reported greater efficacy (P < 0.01) in parenting despite more chaotic home environments (Cohen's d = 0.72) and less frequent supportive parenting, including expressive encouragement (Cohen's d = 0.51), emotion-focused reaction (Cohen's d = 0.64), and problem-focused reactions (Cohen's d = 0.72).

Conclusions: Preschool-aged offspring of father's with ADHD have high rates of ADHD. The child's symptoms may be further exacerbated by disorganization in the home and less supportive paternal parenting. Traditional parenting interventions may need to be modified for use with fathers with childhood ADHD

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J Am Acad Child Adolesc Psychiatry. 2016;55:S200.

IMPACT OF CAREGIVER EXPRESSED EMOTION ON PEDIATRIC PSYCHIATRIC ILLNESS EXACERBATION.

Jalnapurkar IR, Sullivan ZJ, Desai P, et al.

Objectives: Psychosocial stressors, including elevated family stress has been associated with increased relapse among patients with mood and psychotic disorders. The current study was designed to examine the prevalence of high Expressed Emotion (EE) attitudes among primary care givers in acutely hospitalized pediatric patients with Mood, Psychotic, or ADHD/Conduct Disorders, respectively and to also examine the relationship between High EE Ratings and various sociodemographic and clinical variables.

Methods: 41 primary caregivers of children ages 8-17 yr. (14±2.7 yr.) admitted to an acute psychiatric inpatient unit were interviewed within the initial 5 days of admission. The standardized interview consisted of a Five Minute Speech Sample (FMSS) and was subsequently coded utilizing the EE and FMSS coding systems. Sociodemographic (age, gender, race) and clinical data (diagnosis, number of previous admissions, familial psychiatric diagnosis, medication compliance) were analyzed using Chi-square tests and Pearson's correlations.

Results: Results from this sub-group (41 of expected 150 subjects) revealed that over 75 percent (31/41) of the primary caretakers of children and adolescents admitted to the acute psychiatric unit were classified as high EE. While there was no significant relationship between demographic factors and EE ratings, high caregiver EE was associated with increased rate of medication non-compliance ($p<0.05$). There was also a trend for the caretakers of pediatric inpatients with more previous admissions to have elevated EE ratings.

Conclusions: While these results are preliminary, they suggest that more than 3/4 of the caretakers of children and adolescents hospitalized for an acute exacerbation of a primary mood, psychotic, or ADHD/Conduct Disorder were classified with High EE. In addition, medication non-compliance may be the common pathway between high caretaker EE and subsequent relapse in children and adolescents with psychiatric illness. If replicated in the larger sample, this finding may provide further evidence for the importance of family-focused treatment interventions in reducing relapse in children and adolescents with psychiatric illness

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J Am Acad Child Adolesc Psychiatry. 2016;55:S214.

QUANTITATIVE ELECTROENCEPHALOGRAPHY REFLECTS VARIOUS EXECUTIVE FUNCTIONS IN CHILDREN WITH ATTENTION-DEFICIT/ HYPERACTIVITY DISORDER.

Jhung K, Park JY, Choi J.

Objectives: ADHD is a widely prevalent condition in school aged children, and making a precise diagnosis is an important clinical issue. Quantitative EEG (qEEG) has been increasingly used to evaluate patients with ADHD. This study aimed to assess the correlation of qEEG data with various executive performance tasks in patients with ADHD.

Methods: Twenty-two patients with ADHD were recruited. Electroencephalography was assessed in the resting-state, and qEEG data were obtained in both eyes-open and eyes-closed state. Comprehensive Attention Test (CAT), Stroop Color-Word Inference Test (Stroop CWIT), Trail Making Test (TMT), and Wisconsin Card Sorting Test (WCST) were performed. Korean version of the ADHD Rating Scale (K-ARS) and Korean Child Behavior Checklist 6-18 (K-CBCL) was assessed.

Results: In general, alpha, beta and gamma power positively correlated with the Attention Quotient (AQ), while delta and theta power negatively correlated with AQ from CAT. In the Stroop CWIT, delta and theta powers decreased, as alpha, beta and gamma powers increased, in relations to higher performance. Power of the gamma band decreased with higher TMT performance. Moreover, delta, theta and gamma power negatively correlated with good performance on the WCST, while alpha band showed a positive correlation.

Conclusions: Findings suggest that qEEG may be a useful adjunctive tool in assessing patients with ADHD

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J Am Acad Child Adolesc Psychiatry. 2016;55:S324.

LONG-TERM OUTCOMES OF CHILDHOOD ATTENTION-DEFICIT/HYPERACTIVITY DISORDER: THE NEW YORK STUDY.

Klein RG, Castellanos FX, Ramos-Olazagasti M.

Objectives: The goals of this study are to describe long-term clinical and functional outcomes in the New York Study of hyperactive children who were followed prospectively for 33 years and identify possible predictors that influence these outcomes.

Methods: White hyperactive boys (N = 207 probands) were recruited in childhood and followed in adolescence (mean age 18 years), early adulthood (mean age 25 years), and mid-adulthood (mean age 41 years). In late adolescence, 178 comparison participants were recruited. At the final followup in mid-adulthood, a total of 135 probands and 136 comparison participants (65.2 and 76.4 percent of original cohort, respectively) were assessed. Outcome measures included occupational, economic, and educational attainment and marital history, occupational and social functioning, ongoing and lifetime psychiatric disorders, hospitalizations, obesity, risk-taking behaviors, and criminal behaviors.

Results: Compared with peers without ADHD, probands showed greater persistence of ADHD, along with greater prevalence of CD/antisocial personality disorder (APD) and SUD in late adolescence. These dysfunctions continued into early adulthood, even when ADHD remitted for the majority of the sample group, and were associated with deficits in educational and occupational attainment, leading to a relative economic disadvantage. Furthermore, the disproportionally high rate of CD/APD and SUD in probands versus comparison participants translated to significantly higher rates of criminality, risk-taking behavior, and risk-related medical outcomes in adulthood. Probands also showed elevated obesity rates in relation to comparison participants but no differences in mood or anxiety disorders.

Conclusions: There is heterogeneity in the clinical and functional outcomes of children with ADHD. This study's findings show that childhood ADHD does not preclude adequate functioning in various life domains. However, it does predispose to maladjustment in adolescence and adulthood in a subset of these children, particularly those who develop CD/APD, an important predictor of long-term outcome

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J Am Acad Child Adolesc Psychiatry. 2016;55:S217.

A SIX-MONTH OPEN-LABEL MULTICENTER STUDY OF THE SAFETY AND EFFICACY OF PRC-063 IN ADOLESCENTS WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.

Kollins SH, Cutler AJ, Khattak S, et al.

Objectives: This six-month, open label, multicenter, phase 3 study evaluated the long-term safety and efficacy of a novel, extended release formulation of methylphenidate (PRC-063) in adolescents with ADHD.

Methods: One hundred seventy-six subjects (12 to 17 years old) were enrolled following successful completion of a double-blind study. Starting dose was chosen by investigators followed by weekly titration visits until an optimal dose was achieved (25, 35, 45, 55, 70 or 85 mg/day). Safety and efficacy evaluations occurred monthly, including the clinician rated ADHD-5-Rating Scale, the Patient Satisfaction Survey (PSS), Weiss Functional Impairment Rating Scale-Parent (WFIRS-P), Behavior Rating Inventory of Executive Function (BRIEF), Youth Quality of Life (YQoL), Pittsburgh Sleep Quality Index (PSQI) and Columbia Suicidality Rating Scale (C-SSRS).

Results: After 6 months of treatment, the mean dose of PRC-063 was 65 mg/ day. A significant improvement in the mean ADHD-5-RS score was observed compared to baseline (-22.0 (10.90); $p<0.0001$) and end of double-blind (-9.6 (10.37); $p<0.0001$). Subjects had significantly improved executive functioning and functional outcome scores compared to baseline on all subscales (BRIEF and WFIRS-P; $p<0.0001$). Quality of life significantly improved compared to baseline values (YQoL; $p=0.0122$). Subject satisfaction with onset of action, duration of action, level of awareness, ability to fall asleep, lunch appetite, dinner appetite, overall AEs and overall efficacy improved compared with baseline (PSS; $p<0.05$). Sleep quality was not negatively impacted compared to baseline, as measured by the PSQI. Subjects had no observed suicidal behaviors, as measured by the C-SSRS. No clinically significant laboratory, vital signs, or ECG findings or changes were reported. 8 subjects discontinued due to treatment-emergent adverse events (TEAEs). Ninety-seven percent of TEAEs were mild or moderate in severity. Two SAEs occurred, one of which (severe aggressive behavior) was determined to be related to study treatment.

Conclusions: PRC-063 was well-tolerated and effective in the treatment of ADHD in adolescents over a six-month period. ADHD symptom improvement compared to baseline and end of double-blind was observed, as were improvements in functional outcome, executive function, quality of life and patient satisfaction

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J Am Acad Child Adolesc Psychiatry. 2016;55:S218.

THE INFLUENCE OF COMORBID PROBLEMATIC INTERNET USE ON QUANTITATIVE ELECTROENCEPHALOGRAPHY DEVIANCES IN BOYS WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.

Kim JW, Choi TY.

Objectives: ADHD studies, findings related to resting-state quantitative electroencephalogram (QEEG) have been relatively consistent over a long period of time. However, several factors have been shown to influence the QEEG results. One of the important influential factors is an existence of other comorbid psychiatric conditions. The aim of the present study was to evaluate the role of comorbid psychiatric symptom on quantitative EEG (QEEG) activities using an age-matched sample.

Methods: ADHD diagnosis was based on the Korean version of the Diagnostic Interview Schedule for Children Version IV (DISC-IV) and these diagnoses were confirmed by several child and adolescent psychiatrists. Boys with ADHD were assigned to one of three groups: pure ADHD (N=22), ADHD with depressive symptoms (N=11), and ADHD with problematic Internet use (N=19). Typically developing children (N=27) were also enrolled in this study. A resting EEG was recorded during three minutes with the participant's eyes closed. Five frequency bands were defined for further analysis: delta (1-4 Hz), theta (4-8 Hz), alpha (8-12 Hz), beta (12-30 Hz), and gamma (30-50 Hz).

Results: In the repeated measures ANOVA model, a significant main effect of the group was found for the absolute theta power (df=2, F=3.828, p=0.029), with the pure ADHD group exhibiting higher theta power than the ADHD with problematic Internet use. In the follow-up analysis, the absolute theta power was relatively high in the pure ADHD group at the central (C3, T4, and Cz) and posterior (P3, O1, O2, T5, T6, and Pz) regions. The ADHD with depressive symptom group showed no significant differences in any region compared with pure ADHD group and the ADHD with problematic Internet use group.

Conclusions: The ADHD with problematic Internet use group showed increased absolute theta power at the central and posterior regions. However, the ADHD with depressive symptom group had no significant impacts on QEEG activities in any region. These findings will contribute to a better understanding of brain-based electrophysiological changes in boys with ADHD in accordance with comorbid psychiatric symptoms

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J Am Acad Child Adolesc Psychiatry. 2016;55:S27.

INSOMNIA AND ATTENTION-DEFICIT/ HYPERACTIVITY DISORDER: RATIONAL APPROACH TO TREATMENT.

Ivanenko A.

Objectives: Substantial evidence suggests that sleep disturbances are commonly seen in children with ADHD and represent a significant source of stress for the child and family. Sleep problems are frequently reported in clinical practice and in an estimated 25 to 50 percent of children and adolescents who have ADHD. Behavioral, circadian, and genetic models have been suggested to explain the underlying mechanisms associated with the disrupted sleep, bedtime refusal, and long sleep latencies that characterize children with ADHD.

Methods: This session provides a comprehensive literature review, case material, and discussion.

Results: Common sleep problems in children with ADHD include chronic sleep-onset insomnia, bedtime refusal, and primary sleep disorders, including sleep apnea and restless legs syndrome/periodic leg movement disorder. Potential etiological factors for sleep problems associated with ADHD include behavioral, physiological, and genetic components. When presented with the common clinical scenario of sleep complaints in a child or adolescent with ADHD, the mental health provider needs to adopt an organized and step-wise approach to evaluation, in addition to diagnostically driven treatments. Additional considerations involve an assessment of the relative contributions of sleep practices (i.e., bedtime routine, sleep-wake schedules, electronic use at bedtime), comorbid anxiety and mood symptoms, evening

symptoms of ADHD, concomitant medication use, and comorbid sleep disorders such as restless legs syndrome.
Conclusions: A practical approach to addressing sleep problems in children with ADHD using a systematic, evidence-based approach will be presented

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J Am Acad Child Adolesc Psychiatry. 2016;55:S97-S98.

ASSESSMENT AND MANAGEMENT OF ATTENTION-DEFICIT/HYPERACTIVITY DISORDER IN YOUTH WITH AUTISM SPECTRUM DISORDER.

Joshi G, Veenstra-Vander Weele JM.

Objectives: This presentation will offer an up-to-date review of the emerging evidence on the prevalence, clinical characteristics, and management of ADHD in children and adolescents with ASD.
Methods: The literature on ASD was queried to identify published studies on the following: 1) the prevalence and the clinical presentation of ADHD in youth with ASD; and 2) the psychopharmacological interventions for the treatment of ADHD in youth with ASD.
Results: The presentation will open with the information on the prevalence of ASD in nonreferred and in psychiatrically referred populations. The first part of the talk will underscore the burden of psychopathology associated with ASD followed by description of the clinical presentation and recognition of co-occurring ADHD. The second part of the talk will discuss special considerations in the psychopharmacological management of youth with ASD and provide a comprehensive overview of the available evidence on the psychopharmacology of ADHD in ASD. Presentation will emphasize best evidence practice pathways for practical, multimodal treatment of ADHD in the outpatient setting. The concluding portion of the talk will discuss the promising role of glutamate-modulating agents for the treatment of social deficits as well as frequently associated psychopathology, including ADHD, in ASD.
Conclusions: Emerging literature highlights high levels of psychopathology and dysfunction in youth with ASD. Proper recognition of psychopathology in ASD offers opportunity for appropriate medication intervention. An up-to date knowledge of evidence-based pharmacotherapy for ADHD in youth with ASD will help optimize therapeutic interventions

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J Am Acad Child Adolesc Psychiatry. 2016;55:S25.

TO TREAT OR NOT TO TREAT ATTENTION DEFICIT/ HYPERACTIVITY DISORDER IN THE CONTEXT OF SUBSTANCE USE DISORDERS: THAT IS THE QUESTION.

Wilens TE.

Objectives: Clinicians remain confused about the initiation of ADHD treatments (stimulants, nonstimulants, CBT) with regard to SUD. Embedded in this complex issue are concerns of the effectiveness of ADHD treatments, shortand long-term treatment of both ADHD and SUD and the safe administration of medications in context of SUD. The objective of this presentation is to evaluate the international data on treatment and safety of ADHD interventions in relation to SUD.
Methods: A systematic evaluation of the literature was completed. Compiled outcomes from controlled trials and prospective, retrospective, and registry databases were examined. Outcomes for both ADHD and SUD were examined. Both safe administration of ADHD medications (misuse/diversion) and potential adverse effects of ADHD treatments were evaluated.
Results: In adolescents and adults with comorbid ADHD and SUD, data from multiple randomized controlled trials show that lower dose stimulants and nonstimulants may not be particularly effective for either ADHD or SUD. However, more recent data suggest that higher dose stimulants maybe effective in ADHD and SUD. Active SUD worsens ADHD symptoms. Abstinent SUD groups appear to have improved outcomes in both ADHD and SUD associated with treatment. Survey and controlled studies also suggest that, naturalistically, ADHD stimulant medications are often misused in the context of SUD.
Conclusions: Emerging data suggest that current strategies of treating ADHD and SUD need to take into consideration status of recovery, use of nonpharmacological interventions, preparation, and dose of

medications when working with patients with ADHD and SUD. Nonconsideration of treatment in patients with ADHD who have history of SUD does not appear to be substantiated by the contemporary literature

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J Am Acad Child Adolesc Psychiatry. 2016;55:S328.

NEURAL CIRCUITRY UNDERLYING THREE COMMON AND OFTEN CO-OCCURRING CHILDHOOD DISORDERS: AUTISM SPECTRUM DISORDER, ATTENTION-DEFICIT/HYPERACTIVITY DISORDER, AND LEARNING DISORDER.

Margolis A, Milham MP.

Objectives: This symposium examines shared and distinct disturbances in neural circuits underlying three common and co-occurring childhood disorders: autism, ADHD, and a specific learning disorder.

Methods: Presenters will report findings from structural and fMRI studies of learning, attention, and autism spectrum disorders across childhood and adulthood. Dr. Michael Milham will discuss the implications of abnormalities in shared and distinct circuits in comorbid conditions for behavioral assessment and pharmacological and behavioral treatment approaches.

Results: Studies reveal altered connectivity in circuits that underlie overlapping behaviors in distinct disorders (e.g., ADHD and autism) and within subtypes of disorders (e.g., learning disorder in reading versus math). Dr. Adriana DiMartino demonstrates evidence of reduced connectivity between the right fusiform face area and rostral anterior cingulate in children with ADHD who present with traits of autism. Dr. Jonathan Posner demonstrates the dissociation of neural circuits, supporting executive function and emotion regulation in children with ADHD. Dr. Maki Koyoma demonstrates that intrinsic functional connectivity of the left middle frontal gyrus is related differentially to numeracy and literacy in adults. Dr. Amy Margolis reports functional and anatomical abnormalities in temporoparietal cortices in children with reading disorder. Thus, the use of neuroimaging can shed light on how altered function in shared circuits may underlie a number of common childhood disorders with distinct behavioral presentations. This symposium will enable attendees to discuss the normal functioning of neural circuits underlying these childhood disorders and how neuroimaging can shed light on the dimensional and categorical nature of these disorders.

Conclusions: Use of structural and fMRI to test dimensional constructs in sample groups of children with and without comorbid conditions reveals underlying pathophysiology of common childhood disorders. These findings support using a dimensional and categorical approach to understanding psychopathology, which may provide targets for new treatment strategies, whether they are psychosocial or psychopharmacological, aimed at addressing circuit-based disturbances that underlie maladaptive behaviors associated with these childhood disorders

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J Am Acad Child Adolesc Psychiatry. 2016;55:S91.

ATTENTION-DEFICIT/HYPERACTIVITY DISORDER: FROM DIAGNOSIS TO PHARMACOLOGY: WHAT'S NEW?

Wilens TE.

Objectives: The goal of this session is to review articles chosen by the Lifelong Learning Committee addressing current concepts and understanding in the following areas: 1) risk of tics associated with stimulant treatment for ADHD; 2) impact of activity level on working memory and performance in children with ADHD; 3) diagnostic reliability of integrating an EEG biomarker with a clinician's ADHD evaluation; 4) discussion of the ethics and safety related to the use of cognitive enhancers; and 5) the results of a randomized, placebo-controlled trial of guanfacine-extended release for adolescent ADHD.

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 findings: 1) meta-analysis found no significant increase in the risk of new onset or worsening of tics when comparing stimulants with placebo; 2) higher rates of activity level predicted significantly better but not normalized working memory performance for children with ADHD; 3) integration of the EEG biomarker with a clinician's ADHD evaluation improved diagnostic accuracy; 4) physicians are inarguably the gatekeepers for a class of drugs that have yet to be fully evaluated for safety

or efficacy for the purpose of neurological enhancement; and 5) compared with placebo, guanfacine-extended release at doses of up to 7 mg/ day was associated with statistically significant improvements in ADHD symptoms, and no new safety signals were reported.
Conclusions: It is noteworthy that new evidence suggests that hyperactivity in ADHD may actually play a compensatory role in improving working memory. A more accurate diagnosis of pediatric and adolescent ADHD might be achieved by combining EEG biomarkers with clinician evaluation. Treatment of ADHD with stimulants does not necessarily increase the risk of new or worsening tics. Higher dose of guanfacine-extended release is effective in adolescents with ADHD. Although public policy may intervene in the near future, it is currently up to the physician to determine what constitutes best practice for prescribing stimulant medications

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J Am Acad Child Adolesc Psychiatry. 2016;55:S99.
ATTENTION-DEFICIT/HYPERACTIVITY DISORDER: FOCUS ON PHARMACOTHERAPY.
Wilens TE.
Objectives: With the increasing number of presentations of children and adults with ADHD, practitioners are requiring strategies for those individuals with the disorder, as well as those who do not respond or are unable to tolerate traditional treatment.
Methods: A systematic review of the literature was undertaken to elucidate data on stimulant and nonstimulant pharmacological treatments for ADHD simplex and for treatment refractory or comorbid ADHD. Studies using controlled, open, retrospective, and case series will be highlighted and weighted according to the study design. Longer-term outcomes of existing agents and recently published data are favored.
Results: The literature combined with practice parameters and the clinical experience indicates that both stimulants and nonstimulants remain among first-line pharmacotherapy for ADHD in preschoolers, latency/school-aged youth, and adolescents. Alterations in the use of traditional stimulants, the use of nonstimulants, and combinations of medications can enhance a patient's ADHD response. A discussion of predictable (e.g., weight loss) and idiosyncratic adverse effects will be undertaken with recent longer-term data on these treatments presented.
Conclusions: In this session, pharmacological strategies for treating ADHD children and adolescents will be presented, incorporating new research findings and US FDA approvals punctuated by systematic clinical observation

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J Am Acad Child Adolesc Psychiatry. 2016;55:S164-S165.
EFFICACY OF METHYLPHENIDATE EXTENDEDRELEASE CHEWABLE TABLETS IN CHILDREN WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER: OPEN-LABEL, DOSE-OPTIMIZATION PERIOD OUTCOMES.
Wigal SB, Childress AC, Berry S, et al.
Objectives: To further examine the efficacy and safety of open-label (OL) methylphenidate, extended-release chewable tablets (MPH ERCT; 20-60 mg) in children with ADHD during the 6-week, dose-optimization period of a phase 3, laboratory classroom study. Primary outcomes were reported previously.
Methods: Boys and girls (aged 6-12 years) diagnosed with ADHD, with a need for pharmacological treatment in the judgment of the investigator and an ADHD Rating Scale (ADHD-RS-IV) score in the 90th percentile or higher for gender and age at screening or baseline, were enrolled. In the 6-week OL period, MPH ERCT dose was titrated in increments (10-20 mg per day weekly) based on efficacy and tolerability (maximum dose, 60 mg per day). Participants then were randomly assigned to a 1-week double-blind treatment with MPH ERCT or placebo, followed by a laboratory classroom evaluation. Dose optimization period efficacy assessments included the ADHD-RS-IV, Clinical Global Impressions-Severity (CGI-S), Conners' Parent Rating Scale (CPRS), and Clinical Global Impressions-Improvement (CGI-I). Adverse events (AEs) were collected throughout the study.
Results: A total of 90 participants were enrolled. Final optimized daily MPH ERCT dose ranged from 20 to 60 mg (mean = 42.5 mg). Mean age and weight were numerically lower for participants with a 20 mg per day final dose compared with those at higher doses. Treatment with OL MPH ERCT was associated with a

progressive decrease in mean (SD) ADHD-RS-IV total score from 40.1 (8.72) at baseline to 12.5 (7.80) at week 6. Likewise, mean CGI-S score decreased from 4.6 (baseline) to 2.0 (week 6), and mean CGI-I score decreased from 3.0 (week 1) to 1.3 (week 6). Mean change from baseline in CPRS scale scores at week 6 ranged from -6.6 (social problems) to -24.9 (hyperactivity). Treatment-emergent AEs were reported by 65 of 90 (72.2 percent) participants in the OL period. Decreased appetite, upper abdominal pain, mood swings, irritability, insomnia, and upper respiratory tract infection were reported by ΓëÑ10 percent of participants. No serious AEs were reported during the study.
Conclusions: ADHD symptoms were reduced during the 6-week, OL treatment with MPH ERCT (20 to 60 mg per day). Open-label MPH ERCT was generally safe and well tolerated

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J Am Acad Child Adolesc Psychiatry. 2016;55:S296.

EVIDENCE OF A PHARMACOLOGICAL DISSOCIATION BETWEEN THE ROBUST EFFECTS OF METHYLPHENIDATE ON ATTENTION-DEFICIT/ HYPERACTIVITY DISORDER SYMPTOMS AND WEAKER EFFECTS ON WORKING MEMORY.

Spencer TJ.

Objectives: ADHD and working memory (WM) deficits often co-occur but do not define ADHD. Preclinical and neuroimaging studies show that ADHD and WM deficits are dissociated at the level of individual dopamine receptor function in a prenatal nicotine-exposed mouse model of ADHD and in a resting-state fMRI study. The main aim of the present study was to test the hypothesis that there would also be a pharmacological dissociation of the effects of stimulants on ADHD and WM.
Methods: Subjects with ADHD were derived from three previously completed prospective clinical trials involving treatment with extended release methylphenidate (OROS-« MPH) for at least six weeks. Subjects were adolescents and adults with DSM-IV ADHD, with systematic assessments of psychometrically (Cambridge Neuropsychological Test Automated Battery, CANTAB) and behaviorally (Behavior Rating Inventory of Executive Function, BRIEF) defined measures of WM, as well as assessments of ADHD symptoms. Cohen's d was used to evaluate effect size between baseline and week six for all assessments, and Pearson correlations were used to evaluate the relationship between assessments at baseline and between change scores for assessments from baseline to week six.
Results: Cohen's d estimates for the CANTAB spatial working memory measures differed significantly by 1.8 standard deviations (t=-10.8, df = 70, P < 0.001) and 1.9 standard deviations (t= -11.1, df = 70, P < 0.001) for the strategy and total between-errors subcategories, respectively, and confidence intervals did not overlap with those of the Adult ADHD Investigator Symptom Rating Scale (AISRS). A similar effect was observed for changes in AISRS and the BRIEF working memory scale where the Cohen's d estimates differed significantly by 1.1 standard deviations (t = -2.5, df = 137, P = 0.015), and the confidence intervals did not overlap.
Conclusions: These findings provide further evidence for the dissociation between ADHD and WM deficits that often accompany but do not define ADHD

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J Am Acad Child Adolesc Psychiatry. 2016;55:S219-S220.

PHARMACOKINETICS OF A NOVEL, EXTENDED-RELEASE FORMULATION OF METHYLPHENIDATE (PRC-063) IN ADOLESCENTS WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER AND IN HEALTHY ADULTS AT STEADY STATE.

Quinn DM, Bode TD, Donnelly G, et al.

Objectives: Two studies sought to compare the pharmacokinetics of PRC- 063 with immediate-release methylphenidate (IR MPH): Study A a single-dose crossover study in adolescents with ADHD; and Study B a 5-day steady-state crossover study in healthy adults.
Methods: Study A involved adolescents (12-17 years) with a DSM-5 diagnosis of ADHD and receiving a stable dose of MPH. Subjects took a single daily dose of PRC-063 or IR MPH (tid) that was approximate to their pre-study dose. Plasma samples were collected prior to dosing and at 0.5 through to 30 h post-dose. Study B involved healthy adults 18 years of age or older. Subjects received either 100mg of PRC-063 or 60mg of IR MPH (20mg tid) for 5 days. Plasma samples were collected prior to dosing at Day 1, 3, 4 and 5, and on Day 5 at 0.5 through to 36 hours post-dose.

Results: Study A enrolled 17 patients (3 female, 14 male, age 14.0±1.0 yrs). The mean daily dose was 62.9 mg/day of PRC-063 and 54.7 mg/day of IR MPH. For d-methylphenidate non-dose-normalised data, the ratios of leastsquares means of PRC-063:IR MPH for ln-transformed AUC0-t, AUC0-inf and Cmax were 96.66%, 100.76% and 67.06%, respectively. Residual levels of MPH at 24 h post dose were 3.28 ng/mL for PRC-063 and 0.53 ng/mL for IR MPH. Study B enrolled 21 subjects (9 female, 12 male, age 32±8 yrs). There were two distinct peak plasma levels of MPH for PRC-063 (1.5 and 12 h post dose) and three for IR MPH (2, 5.5 and 10 h post dose). Fluctuation Index was 131.5±31.9% for PRC-063 and 243.53±34.0% for IR MPH. For d-methylphenidate dose-normalised data, the ratios of least-squares means of PRC- 063:IR MPH for AUC0-24, Cmax and Cmin were 88.57 percent, 59.35 percent and 274.15 percent, respectively. Steady-state was achieved for PRC-063 by Day 3. No new safety signals were identified in these studies.
Conclusions: In both studies, the extent of absorption was comparable between PRC-063 administered as a single dose and IR MPH administered three times; however, the rate of absorption was lower for PRC-063. No evidence of unusually rapid release was observed compared to IR MPH. PRC- 063 provides a once-daily alternative to tid administration of MPH with less peak to trough fluctuation and higher plasma levels from hour 12 to the end of the day

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J Am Acad Child Adolesc Psychiatry. 2016;55:S222-S223.

COMPLEXITY OF IDENTIFYING ATTENTION-DEFICIT/ HYPERACTIVITY DISORDER AND COMORBIDITIES IN A DISADVANTAGED LATINO POPULATION.

Spencer A, Chiang C, Plasencia N, et al.

Objectives: Underserved, minority children are at risk for under-identification of ADHD and comorbidities, and suffer disproportionately from poor outcomes. The goal of this study was to evaluate the clinical validity of parent report screening tools to identify ADHD and comorbidities in a sample of socioeconomically disadvantaged Latino children referred for psychiatric consultation, and to examine the effect of demographics on scores and diagnoses.
Methods: Variables extracted by chart review included demographics, diagnoses, and standardized questionnaire results. Analyses assessed agreement between the Pediatric Symptom Checklist Attention Scale (PSC-AS), Child Behavior Checklist ADHD Subscale (CBCL-ADHD), and ADHD diagnosis by a child psychiatrist.
Results: Over half of patients were referred for ADHD symptoms, and ninety of the 157 patients evaluated were diagnosed with ADHD, almost all with comorbidities and more than half with multiple comorbidities. Patients with non-English speaking parents were less likely to have completed PSC's and had lower PSC-AS scores. All measures using recommended cut-offs had low sensitivity for ADHD. The PSC-35 had the strongest association with ADHD diagnosis and was least affected by comorbidity, while the CBCL-ADHD scale was more sensitive to highly comorbid ADHD. Using Receiver Operating Characteristics (ROC) curve analysis with the PSC-AS data, a cut-off of 3 provided the most balanced sensitivity and specificity trade-off (sensitivity 0.87, specificity 0.49).
Conclusions: Findings suggest that parent-report tools using published cutoff scores have low sensitivity in this population and that non-English speaking parents may under-report symptoms. Therefore, disadvantaged Latino children with ADHD may not be recognized and not treated. Pediatricians should consider using the PSC-35 to screen for ADHD with a lower cut-off point on the PSC AS subscale, followed by careful evaluation to assess for comorbidities. Further research is needed to improve the evaluation of ADHD in disadvantaged, Latino children, and to understand the impact of acculturation and education on diagnosis

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J Am Acad Child Adolesc Psychiatry. 2016;55:S131.

PREFRONTAL AND PARIETAL CORRELATES OF COGNITIVE CONTROL RELATED TO THE OUTCOME OF ATTENTION-DEFICIT/ HYPERACTIVITY DISORDER DIAGNOSED IN CHILDHOOD.

Schulz KP, Li X, Clerkin S, et al.

Objectives: The protracted and highly variable development of prefrontal cortex and the cognitive control processes supported by the region have been purported to be a major determinant of the adult outcome of ADHD. This neurodevelopmental model was tested in a prospectively followed sample group of adults ages 21-28 years who were diagnosed with ADHD in childhood.

Methods: Twenty-seven adult probands diagnosed with ADHD in childhood and 28 carefully matched comparison subjects performed the stimulus and response conflict task during fMRI. Probands were classified with persistent ADHD (n = 11) or remitted ADHD (n = 16). Behavioral and neural responses to stimulus, response, and combined conflicts were compared in probands and comparison subjects and in probands with persistent and remitted ADHD.

Results: Response speed and accuracy for stimulus, response, and combined conflicts did not differ across groups. Orbitofrontal, inferior frontal, and parietal activation was lower in probands than comparison subjects, but only for combined conflicts when demand for cognitive control was highest. Reduced activation for combined conflicts in probands was almost wholly attributable to the persistence of ADHD; orbitofrontal, inferior frontal, anterior cingulate, and parietal activation was lower in probands with persistent ADHD than both probands with remitted ADHD and comparison subjects; however, it did not differ between probands with remitted ADHD and comparison subjects.

Conclusions: These results provide the first evidence that inferior prefrontal and superior parietal activation during cognitive control differs as a function of the persistence or remission of ADHD in adulthood, with persistence linked to reduced activation (as seen in children with ADHD) and remission of symptoms associated with activation similar to comparison subjects without a history of ADHD

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J Am Acad Child Adolesc Psychiatry. 2016;55:S225.

IMPACT ON THE FAMILY UNIT OF EARLY-MORNING FUNCTIONING IMPAIRMENTS IN STIMULANT-TREATED CHILDREN AND ADOLESCENTS WITH ATTENTION-DEFICIT/ HYPERACTIVITY DISORDER.

Schachar RJ, Barkley R, Faraone SV.

Objectives: To assess the impact of Early Morning Functioning (EMF) impairments on the family unit (caregivers, spouse, and siblings) in stimulanttreated children/adolescents with ADHD compared with families of children without ADHD.

Methods: An online quantitative survey was conducted with parents (ΓëÑ65 percent) and/or primary caregivers (referred to as caregivers) of children/ adolescents (aged 6-17 years) with or without ADHD (referred to as children/child). Caregivers of children with ADHD answered qualifying questions to ensure: 1) their child was currently taking a stimulant as the primary ADHD medication; 2) their child was taking a stable dose for ΓëÑ3 months prior to the survey; and 3) they rated their child's ADHD symptoms during the Early Morning Routine (EMR)-defined as the moment the child awakens to the time they leave for school-as ΓëÑ2 on a 10-point Likert severity scale, with 1 denoting ΓÇ£mildΓÇØ and 10 denoting ΓÇ£severeΓÇØ. All eligible caregivers were then asked to rate the severity and frequency in family dysfunction resulting from their child's EMF impairments during the EMR.

Results: There were 330 caregivers of children with ADHD who met the first 2 criteria above, and 300 who met all inclusion criteria (91 percent of sample) and completed the survey. Fifty caregivers of children without ADHD also completed the survey. The severity of EMF impairments during the EMR was significantly higher in families of children with ADHD vs. families of children without ADHD (6.2 vs. 1.5, respectively). The majority of caregivers reported their child's early morning ADHD symptoms (87 percent) and impairment of EMF (77 percent) as moderate to severe (rating of 5-10). Caregivers of children with ADHD reported a higher severity (up to 6-fold higher) and frequency (up to 7.6-fold higher) in family dysfunction on all measured domains during the EMR resulting from their child's inadequately controlled ADHD symptoms compared to caregivers of children without ADHD.

Conclusions: To the best of our knowledge, the findings herein are the first to demonstrate that caregivers of children with ADHD report more severe and frequent family dysfunction as a result of their child's

inadequately controlled ADHD symptoms and related EMF impairments during the EMR compared to caregivers of children without ADHD

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J Am Acad Child Adolesc Psychiatry. 2016;55:S221.

ABSENCE OF ALIGNMENT OF SYMPTOM RESPONSE/REMISSION WITH FUNCTIONAL OUTCOMES IN CHILDREN AND ADOLESCENTS FOLLOWING TREATMENT FOR ATTENTION-DEFICIT/ HYPERACTIVITY DISORDER.

Weiss MD, Childress AC, Mattingly G, et al.

Objectives: The objective of this study was to evaluate functional characteristics of children with ADHD and compare the relationship between clinical response/remission and functional outcomes after 11 weeks of treatment with Aptensio XR-« (methylphenidate hydrochloride extended-release capsules; MPH-MLR).

Methods: Data used in this post-hoc analysis were from the open-label (OL) dose-optimization phase (11 weeks) of a pivotal trial. Weiss Functional Impairment Rating Scale (WFIRS) and ADHD Rating Scale (ADHD-RS-IV) were assessed at Baseline and end of OL. Symptom improvement was defined as Γëѐ30 percent decrease in ADHD-RS-IV total score; symptom remission was defined as ADHD-RS-IV total score Γëñ18; functional improvement was defined as change in WFIRS total 0.25 (minimally important difference); and functional remission was defined as WFIRS total 0.65.

Results: At baseline, ADHD-RS-IV mean total scores for treatment naive (n=148) were similar to those for previously treated (n=73; 36.0 vs 36.4); mean WFIRS total indicated more functional impairment for treatment naive (0.82 vs 0.70, p=0.01). WFIRS total and individual domain scores were similar for children vs adolescents. ADHD presentation most prevalent: combined (2/3 of patients) with predominately inattentive being most of the remaining 1/3. Functional impairment was prevalent across WFIRS domains; greatest impairment in Learning (Learning 1.73, Family 0.81, School Behavior 0.62, Life Skills 0.98, Self-concept 0.82, Social 0.64, Risky Activities 0.36). At OL end, statistically and clinically significant improvement in all functional domains was noted (p<0.001). The largest improvement was in learning (1.03 at OL end). Fifty-four percent of patients had functional improvement at OL end, yet 43 percent of patients with symptom improvement did not have functional improvement. Although mean WFIRS total score at OL end for those with symptom remission was 0.45, 19 percent with symptom remission remained functionally impaired.

Conclusions: Children and adolescents with symptom improvement or remission following treatment with MPH-MLR did not consistently show functional improvement or normalization, which demonstrates the importance of including functional outcomes in clinical studies. Children who continue to show significant functional impairment despite symptom normalization may require additional therapeutic interventions

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J Am Acad Child Adolesc Psychiatry. 2016;55:S161.

DIFFERENCE OF FACIAL EMOTION RECOGNITION AND DISCRIMINATION BETWEEN CHILDREN WITH ATTENTION-DEFICIT/ HYPERACTIVITY DISORDER AND AUTISM SPECTRUM DISORDER.

Lee JS, Kwack YS.

Objectives: This study aimed to investigate the differences in facial emotion recognition and discrimination between children with ADHD and ASD children.

Methods: 53 children, aged 7 to 11 years participated in this study. Among them, 43 were diagnosed with ADHD, according to DSM-IV-TR and K-SADS-PL. And 10 were diagnosed with ASD, according to DSM-IVTR. The parents of the participants have completed the Korean version of Child Behavior Checklist (K-CBCL), ADHD Rating Scale, Conner's scale. The participants have completed Korean Weschler Intelligence Scale for Children forth edition (K-WISC IV) and Advanced Test of Attention (ATA), Penn Emotion Recognition Task(ER40) and Penn Emotion Discrimination Task (EDF40). ER40 and EDF40 are parts of the University of Pennsylvania Computerized Neuropsychological Test Battery. Group differences on facial emotion recognition and discrimination were analyzed by using analysis of covariance(ANCOVA) controlling for visual omission error index in ATA.

Results: There was no group difference in K-CBCL, K-WISC IV and ATA, except rule-breaking behavior scale in CBCL(P=0.048) and visual omission error index in ATA(P=0.005). ADHD children were found to

have better ability in the recognition of happy(p=0.019) and sad faces(p=0.043), and showed less false positive neutral response(p=0.015) than ASD children. No group differences were found for angry, fear, and neutral faces. ADHD children responded faster than ASD children when they showed correct responses(p=0.035). Also, ADHD children recognized emotion better than ASD children on female faces(p=0.025), but not on male faces. And ADHD children showed better(p=0.009) and faster response(p=0.037) than ASD children in the recognition of extreme emotional expression, but there was no difference in the recognition and response time of mild emotional expression. We found no statistically significant difference in the discrimination of facial emotional intensity between the children with ADHD and ASD children.
Conclusions: The findings in this study suggested that children with ADHD recognize facial emotion better than children with ASD, but still have deficit in emotional recognition. Intervention which considering different ability of emotional recognition and discrimination is needed

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J Am Acad Child Adolesc Psychiatry. 2016;55:S263-S264.

A SMART DESIGN EXAMINING THE IMPACT OF CNS STIMULANTS ON THE GROWTH TRAJECTORIES OF CHILDREN WITH ATTENTION DEFICIT/ HYPERACTIVITY DISORDER .

Waxmonsky JG.

Objectives: There is increasing evidence that central nervous system (CNS) stimulants may lead to growth suppression in children who are prescribed these drugs long-term to treat ADHD. Few studies have used unmedicated youth with ADHD for comparison; previous work primarily has examined the effects of immediate release stimulants often in previously treated children. Emerging evidence suggests that inconsistent medication usage produces less suppression than consistent usage throughout adolescence. However, the impact of drug holidays on growth and the efficacy of other clinical interventions to improve weight gain, such as caloric supplementation, have not been examined systematically. A sequential, multiple assignment, randomized trial (SMART) design was used to assess the effects of extended release CNS stimulants on growth in treatment naive youth with ADHD, including the efficacy of common clinical interventions to improve weight gain and growth in children experiencing weight loss after initiation of CNS stimulants.
Methods: An adaptive intervention was used to mimic clinical practice where efforts to improve weight gain in children with ADHD occur after evidence of weight loss or growth suppression is seen.
Results: Treatment medication naïve youth with ADHD (n = 230) were assigned randomly to either treatment with extended release methylphenidate (ER-MPH) and a low-intensity behavioral intervention (78 percent) or more intense behavioral services without pharmacological treatment (22 percent). Weight, height, ADHD symptoms, and impairment were measured biweekly until medication was optimized (a maximum of 12 weeks), then monthly for 3 months, and then at least every 3 months for a total of 30 months. Treatments for ADHD were provided through the study with 142 participants optimized on medication dose. After 6 months, children showing meaningful reductions in BMI (N = 73) were assigned randomly to one of three weight promotion arms: 1) monthly weight monitoring (active control arm); 2) limiting medication to school hours (drug holiday); or 3) addition of a 150-kcal supplement, with continuation of daily usage of ER-MPH. Participants were maintained in the second randomized assignment until they reached a target BMI.
Conclusions: The presentation will discuss the rationale and relative benefits of the SMART design for addressing study aims, as well as methodical considerations for implementing the design

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J Am Acad Child Adolesc Psychiatry. 2016;55:S212.

PREDICTION OF IMPAIRMENT IN SCHOOL FUNCTION OVER ONE SCHOOL YEAR IN SPECIAL EDUCATION STUDENTS WITH PSYCHIATRIC DISORDERS.

Mattison RE.

Objectives: Functional impairment in school is routinely measured by grade point average (GPA), absenteeism, and suspensions. The purpose of this study was to determine for students with psychiatric disorders those variables that could predict the worst dysfunction on these measures over a school year,

thus identifying the most at-risk students to school staff, and suggesting more specific targets for interventions.
Methods: A cohort of 196 students in a self-contained public school for secondary special education students with psychiatric disorders was followed over one school year. By the end of the first marking period the following information was available: demographics, IQ, reading and math achievement, and teacher ratings of psychopathology. Logistic regression analyses were then used to identify predictors for the worst final dysfunction in GPA, absenteeism, suspensions, and psychiatric inpatient/partial hospitalization during the school year.
Results: The most dysfunctional groups were established for each area: GPA of <70 (29.6 percent), absenteeism of >24 days (33.2 percent), any suspension (36.2 percent), and any psychiatric inpatient/partial hospitalization (28.6 percent). The resultant significant predictors for each most impaired group were: GPA (non-Caucasian, low Verbal IQ, and high ADHD-Inattentive scale; concordance = 76.7 percent); absenteeism (older and high Social Anxiety scale; 71.3 percent), suspension (high Conduct Disorder scale; 75.7 percent), and hospitalization (younger and high Depression scale; 67.5 percent).
Conclusions: Information that child psychiatrists can easily obtain for their special education students with psychiatric disorders can produce practical results that can benefit both their patients and school staffs to whom they consult. For example, academically, non-Caucasian students with decreased language skills and attention appeared to be most at-risk for poor GPA. Consequently, clinicians and school staffs could ensure optimal treatment for such students in any ADHD, language disorders, and accompanying learning disorders in reading and/or writing. The results further model how practical research can be conducted in schools, as well as increase the limited evidence base that school consultants can use to assist their patients and special education colleagues

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J Am Acad Child Adolesc Psychiatry. 2016;55:S142.

ASSESSMENT OF CLINICIAN'S KNOWLEDGE AND SCREENING PRACTICES OF NON-MEDICAL STIMULANT USE IN PATIENTS WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.

McCoy MA, Randall TL.

Objectives: According to SAMHSA, the number of prescriptions for stimulants dispensed by U.S. retail pharmacies have increased 8-fold from 4 million in 1991 to 29 million in 2009. As the first line of treatment for ADHD, stimulants have a significant rate of misuse, with studies showing students in grades 8-12 as having a lifetime prevalence of nonmedical use of stimulants of 9.1 percent. Clinicians should be aware of the potential for misuse when prescribing stimulants, especially with increasing number of stimulants dispensed. It is incumbent that prescribers discuss issues about diversion and misuse with their patients. This study will assess the knowledge on stimulant misuse and clinician's practice for screening for stimulant misuse.
Methods: A subset of clinical prescribers will complete a short survey on both their knowledge of stimulant misuse and their practice of screening for stimulant misuse.
Results: We will obtain information on the level of training and familiarity with stimulant misuse and screening. We anticipate that prescribers will have a moderate understanding of the issues surrounding stimulant misuse; however, the use of a consistent screening practice and assessment will be low based on the multiple demands of clinical care.
Conclusions: We anticipate that education and training around nonmedical stimulant use and training on ways to screen for misuse would be helpful for prescribers. Having regular conversations with patients over age 12 years and with their parents about misuse and diversion along with prescribing long-acting formulations for high risk individuals may help decrease stimulant misuse. A best practice alert embedded into an electronic medical record to remind practitioners about these steps may also be helpful

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J Am Acad Child Adolesc Psychiatry. 2016;55:S216.

EFFECT OF ATOMOXETINE ON HEIGHT AND WEIGHT IN KOREAN CHILDREN AND ADOLESCENTS WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER: A RETROSPECTIVE CHART REVIEW.

Yoon JS, Kweon K, Kim SO, et al.

Objectives: To investigate the effect of atomoxetine on growth in Korean children and adolescents with attention-deficit/hyperactivity disorder (ADHD).

Methods: The medical records of 78 subjects (mean age 9.2 ± 2.0 years; 60 boys) with ADHD who received treatment with atomoxetine for at least 1 year at the Department of Psychiatry at Asan Medical Center were retrospectively reviewed. Height and weight were prospectively obtained and retrospectively gathered. Height and weight were converted to age- and gender-corrected standard scores (z scores) using norms from the Korean population. Growth changes were analyzed from the starting to the end of treatment using random coefficients models with change in weight or height z score as the dependent variable.

Results: Weight z score decreased during the first year of medication (± = -0.098, p = 0.047), and increase after the first year (± = 0.214, p < 0.001). Height z score decreased during the first year of medication (± = -0.060, p = 0.037), and showed no significant change after the first year (± = -0.007, p = 0.834). Changes of weight z score (± = 0.030, p = 0.442) and height z score (± = -0.039, p = 0.123) were not significant during whole treatment period.

Conclusions: These results suggest that treatment with atomoxetine lead to minor reductions in expected height and weight during the first year of treatment. However, the effects tend to be attenuated over time and no significant effect on final height and weight was found. Because of the limitations of this study such as retrospective design, selection bias and high attrition rate, further prospective studies are needed

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J Am Acad Child Adolesc Psychiatry. 2016;55:S209-S210.

ASSESMENT OF COGNITIVE FUNCTIONS AND COMORBID PSYCHIATRIC DISORDER IN CHILDREN AND ADOLESCENTS DIAGNOSED WITH CONGENITAL HYPOTHYROIDISM.

Yildiz N, Gorker I, Demir N.

Objectives: In our study, we aimed to evaluate comorbid psychiatric disorders and subtest with Wechsler Intelligence Scale for Children (WISC-R) in children and adolescents with congenital hypothyroidism (CH) to observe difficulties in cognitive areas, even though they were treated in an early period.

Methods: Patients (aged 6-16 years; N = 40) with a diagnosis of CH, who were examined and treated by Pediatric Endocrinology at Trakya University, participated in the study. Patients with chronic medical diseases, ASD, and psychotic disorders were excluded from the CH group. Forty healthy children without any psychiatric and physical disorders were part of the healthy control group. KSADS for School Age Children was used to determine psychopathologies in the study and control groups. WISC-R, which is usually used to identify both intelligence quality and difficulties in cognitive areas, was performed on the children aged 6-16 years.

Results: Sex distribution was equal in patient and control groups (23 girls, 17 boys in both groups). There was no significant difference in age between the two groups. Full-scale IQ, verbal IQ, performance IQ, and all subtests were significantly lower in subjects with CH than the healthy group. When two groups compared full scale IQ, verbal IQ, performance IQ, information, arithmetic, vocabulary, digit span, and block design, object assembly was found to be significantly lower (P < 0.0001). There was also a significant difference between the two groups in similarities (P = 0.001), comprehension (P = 0.009), picture completion (P = 0.001), picture arrangement (P = 0.018), and coding (P = 0.001). Patients (N = 40) with CH also had other disorders as follows: seven with ADHD, five with enuresis nocturna, three with separation anxiety, five with a learning disability, three with borderline intellectual disability, four with ODD, two with depressive disorder, three with specific phobias, one with mild intellectual disability, one with PTSD, and one with TD. More than one psychiatric disorder was seen in 10 patients. There was a correlation between lower full-scale IQ score and psychiatric disorder potential.

Conclusions: Even though cognitive functions were found to be significantly lower in the CH group than the healthy group, learning and attention problems were found more often than intellectual disability. In addition, there were more externalizing problems than internalizing problems

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J Am Acad Child Adolesc Psychiatry. 2016;55:S216-S217.

AFFECTIVE INSTABILITY AND OPPOSITIONAL DEFIANCE IN ATTENTION-DEFICIT/HYPERACTIVITY DISORDER: TREATMENT EFFECTS.

Krone B, Hildebrandt TB, Bedard AC, et al.

Objectives: ADHD is frequently observed with Oppositional Defiant Disorder (ODD) comorbidity and also with dysregulated emotional processing resulting in mood lability, in absence of mood disorder diagnoses. While this triad of symptoms responds to stimulant drugs in some youth, mood lability and irritability are well-documented side effects of both stimulant and non-stimulant medication treatment for ADHD, and may impact treatment outcomes. This study examines the influence of changes in mood lability on symptoms of oppositional defiance among a large sample of youth with ADHD enrolled in a comparator trial using Atomoxetine and Methylphenidate

Methods: We performed retrospective, descriptive analyses on data for a sample of N=232 youth ages 7 to 17 years old (M=10.4 years, SD=2.72), N=169 (72.7 percent) male, diagnosed with ADHD any subtype, with or without ODD, who were randomized into a multi-site, comparator treatment trial. Presence of mood disorder was exclusionary for this study, and we examined symptoms of mood lability in absence of these diagnoses. We developed a regression model to examine the impact of change in mood lability and ADHD symptoms on symptoms of ODD, and to assess differences by drug, controlling for baseline ratings of symptom severity

Results: Both drugs significantly changed mood lability (b=-.2131, SE=.0816, t=-2.6107, p=.0094) and reduced oppositionality (b=-8.1129, SE=1.4405, t=- 5.6321, p=.0000), with a weak trend favoring MPH; Est=-41.5 (23.2), p=.080) in overall effect. Change in mood lability contributed to approximately 26% of change in oppositionality (r=.258, p<.000), and ADHD symptom reduction accounted for approximately 28% of decrease in oppositionality (r2=0.275, p<.000). The direct effect of mood instability on ADHD response was nonsignificant for both drugs, although the range was large and may account for individual tolerability in response to treatment

Conclusions: Mood lability and oppositionality are commonly associated with ADHD. Treatment for ADHD improves oppositionality, but presence of mood lability may respond more heterogenously. Overall, improvements in mood and ADHD symptoms reduced oppositionality when either drug was used

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J Am Acad Child Adolesc Psychiatry. 2016;55:S216.

CLINICAL AND NEUROPSYCHOLOGICAL CHARACTERISTICS OF ATTENTION-DEFICIT/HYPERACTIVITY DISORDER ACCORDING TO DSM-5 AGE-OF-ONSET CRITERION IN KOREAN CHILDREN AND ADOLESCENTS.

Yoon JS, Lee T, Park KJ, et al.

Objectives: In DSM-5 for ADHD, the age-of-onset criterion has been changed from impairment present before age 7 years to symptoms present prior to age 12 years. This study aimed to compare the clinical features and neuropsychological profiles of children and adolescents with ADHD according to age of onset.

Methods: Participants were recruited from September 2012 to February 2015 at the Pediatric Psychiatry clinic in Asan Medical Center (Seoul, Korea). ADHD subjects were divided into two groups based on the age of onset: onset before age 7 years (early onset) and onset between ages 7 and 12 years (late-onset). The control group was recruited through an internet bulletin board.

Results: The study population consisted of 86 subjects with early onset ADHD (age = 7.6 ± 2.1 years, 65 boys); 58 with late-onset ADHD (age = 9.3 ± 2.3 years, 43 boys), and 88 control subjects (age = 9.1 ± 2.6 years, 45 boys). Both early onset and late-onset ADHD groups had significantly more symptoms and functional impairments than the control group. Mean scores of the ADHD Rating Scale; Parent General Behavior Inventory; majority of the subscales of the Social Responsiveness Scale and the Hyperactivity

subscale of Korean Personality Rating Scale for Children; and Omission Errors on the visual continuous performance test were significantly higher in the early onset and late-onset ADHD groups than in the control subjects.
Conclusions: Our results suggest that the late-onset ADHD group, as defined in DSM-5, has comparable symptom severity, functional impairment, and neuropsychological deficits to those of the early onset ADHD, which is in support of extending of age-of-onset criterion.

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J Am Acad Child Adolesc Psychiatry. 2016;55:S163.
MEDICAL AND PSYCHIATRIC COMORBIDITIES IN KOREAN CHILDREN AND ADOLESCENTS WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.
Kweon K, Park KJ, Lee JS, et al.
Objectives: The objective of this study was to investigate the medical and psychiatric comorbidities of Korean children and adolescents with ADHD.
Methods: This study used the Korean National Health Insurance Review and Assessment Service-National Patient Sample (HIRA-NPS) data in 2011. We used information on 2,140 children and adolescents (age 10.9± 3.1 years, 1,710 boys)who had A DHD(ICD-10: F90) and219,410childrenandadolescentswhodid not have ADHD(age 12.4±3.7 years, 113,704 boys). We compared demographic information with medical and psychiatric comorbidities of the two groups. We weighted logistic regression for calculating odds ratio between two groups.
Results: Most medical comorbidities were frequent in subjects with ADHD. Disease of nervous systems (OR = 2.59, 95% CI 2.52-2.66) was almost three times more frequent than in non-ADHD subjects, followed by endocrine, nutritional, and metabolic diseases (OR = 2.09, 95% CI 2.04-2.15); congenital malformations, deformations, and chromosomal abnormalities (OR = 2.00, 95% CI 1.90-2.11); disease of circulatory systems (OR = 1.79, 95% CI 1.71-1.87); and disease of the blood and blood-forming organ and certain disorders involving the immune mechanism (OR = 1.78, 95% CI 1.70-1.86). Compared with non-ADHD subjects, oppositional defiant and conduct disorders were most prevalent in subjects with ADHD (OR = 81.88, 95% CI 79.00- 84.86). Specific learning disorder (OR = 75.61, 95% CI 69.69-82.04), depressive disorder (OR = 55.76, 95% CI 54.44-57.11), tic disorder (OR = 51.20, 95% CI 49.75-52.68), and bipolar disorder (OR = 50.10, 95% CI 47.56-52.76) followed.
Conclusions: This study suggests that children and adolescents with ADHD have more medical and psychiatric comorbidities than those without ADHD using nationwide population-based data in Korea

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ATTENTION-DEFICIT/HYPERACTIVITY DISORDER TRAJECTORIES IN A LARGE BIRTH COHORT FROM A DEVELOPING COUNTRY.
Rohde LA.
Objectives: The goal of this study is to investigate ADHD trajectories in a population-based longitudinal study.
Methods: Participants belonged to the 1993 Pelotas Birth Cohort Study, including 5,249 individuals born in Pelotas, Brazil, in 1993. They were followed up to age 18 and 19 years, with 81.3 percent retention. The ADHD status first was ascertained at age 11 years using a screening instrument (Hyperactivity Subscale of the Strength and Difficulties Questionnaire) calibrated for DSM-IV ADHD diagnosis based on clinical interviews with parents using the Development and Well-Being Assessment (DAWBA). At age 18-19 years, ADHD diagnosis was derived using DSM-5 criteria, with the exception of age of onset. We estimated the overlap between these groups assessed at ages 11 and 18-19 years, respectively, and the rates of markers of impairment in these two groups compared to subjects without ADHD.
Results: We found ADHD prevalence rates of 8.9 percent in childhood and 12.2 percent in young adulthood (without using the age-of-onset criterion). Both groups had increased levels of impairment in adulthood, as measured by traffic accidents, criminal behavior, incarceration, suicide attempts, and comorbidities.

However, only 17.2 percent of children with ADHD continued to have ADHD as young adults, and only 12.6 percent of young adults with ADHD had the disorder in childhood.
Conclusions: Our findings do not support the premise that adult ADHD is necessarily a continuation of childhood ADHD

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J Am Acad Child Adolesc Psychiatry. 2016;55:S110-S111.

IS THERE AN OVERLAP IN ORGANIZATIONAL SKILLS IMPAIRMENT AMONG CHILDREN WITH AUTISM SPECTRUM DISORDER AND ATTENTION DEFICIT/ HYPERACTIVITY DISORDER?

Roth ME, Stanislawski E, Doggett R, et al.

Objectives: Organization, time management, and planning (OTMP) difficulties have an impact on a substantial proportion (50 percent) of children with ADHD, and they improve with behavioral intervention. Given symptomatic overlap between ASD and ADHD, children with ASD may also experience OTMP impairments. To date, examinations of this domain in ASD are missing. Objectives include the following: 1) to characterize the nature and extent of OTMP deficits in children with ASD and identify rates of ADHD comorbidity in children with ASD with and without OTMP impairments (ASD+, ASD-, respectively); and 2) to identify similarities and differences between the ASD+ and ASD- subgroups and children with ADHD and OTMP impairments (ADHD+).
Methods: We examined data (N = 85) of children aged 8-13 years with DSM-IV-TR diagnoses of ASD (n = 35) or ADHD (n = 31), as well as typically developing children (TDC) (n = 19). ANOVA compared the groups on parent scores on the Children's Organizational Skills Scale (COSS-P) and the subgroups on ASD traits, ADHD traits, and executive functions (ratings on the Social Responsiveness Scale, Conners' Parent Rating Scale, and Behavior Rating Inventory of Executive Functions). A threshold for significance was set at P = 0.01.
Results: Children with ASD and ADHD had higher (i.e., more severe) COSS-P Total T scores than TDC. Forty-two percent of the children with ASD were ASD+ (i.e., COSS-P Total T >65), and 47 percent were categorized as ADHD+. Eighty-seven percent of the ASD+ had comorbid ADHD per clinician's interview, in contrast with only 27 percent of the ASD- subgroup. The severity of ADHD traits and executive dysfunction was no different between ASD+ and ADHD+ groups. In contrast, ASD- children had significantly lower ratings of ADHD and executive function severity than children with OTMP deficits. It is noteworthy that the ASD+ and ASD- groups differed in ASD ratings. Results were replicated with a second, independent sample group (N = 150).
Conclusions: A substantial proportion of children with ASD exhibited OTMP functional impairment difficulties, which accompanied other symptoms typically observed in ADHD. Given the availability of evidence-based interventions for OTMP impairments in ADHD, adaptations of this intervention for this population may be warranted

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J Am Acad Child Adolesc Psychiatry. 2016.

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. 2016;55:S160.

INTERNALIZING PROBLEMS AND ATTENTION-DEFICIT/HYPERACTIVITY DISORDER: A LONGITUDINAL TWIN STUDY OF ETIOLOGY AND GENDER EFFECTS.

Noren Selinus EGM.

Objectives: ADHD often co-occurs with internalizing disorders, such as depression and/or anxiety. A clear understanding of the etiologic mechanisms behind this co-occurrence is hampered by the limited knowledge of the impact of ADHD on internalizing disorders from childhood into adolescence. We aimed to explore this relationship further in this twin study.
Methods: We used a cohort of 4,635 Swedish twins with data collected at ages 9 (or 12) and 15 years. We regressed internalizing problems at age 15 years on ADHD and internalizing problems from the previous age 9 or 12 years, both separately and simultaneously. In a genetically sensitive longitudinal design, we decomposed the variation in internalizing problems at age 15 years into effects carried over from ADHD and internalizing problems at the prior time point, as well as new effects.
Results: There was a positive association between ADHD and internalizing problems in both boys and girls. The longitudinal analysis suggested that internalizing and ADHD symptoms in childhood explained the variance in internalizing problems in adolescent boys and girls in different ways. In girls, ADHD symptoms at baseline predicted internalizing problems at follow-up stronger than in boys. In girls, genetic effects for ADHD at age 9 or 12 years explained 11 percent (95% CI 6-19) of internalizing problems at age 15 years. In boys, the genetic effects for ADHD at baseline only explained 1 percent of internalizing problems at age 15 years. At age 15 years, new genetic effects contributed substantially to internalizing problems in both genders [girls: 30 percent (95% CI 22-38); boys: 35 percent (95% CI 26-42)]. New nonshared environmental effects accounted for a little more than half of the variation in internalizing problems at age 15 years in both genders.
Conclusions: There was a gender difference in the genetic explanation of internalizing problems at age 15 years. In both genders, both new genetic and environmental factors emerged in adolescence

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J Am Acad Child Adolesc Psychiatry. 2016;55:S223.

EFFECTS OF LONG-ACTING METHYLPHENIDATE ON NESFATIN-1 LEVELS IN MALE CHILDREN WITH ATTENTION-DEFICIT/ HYPERACTIVITY DISORDER.

Toz HI, Yalcin O, Adaletli H.

Objectives: Underlying pathophysiological mechanisms of appetite and weight loss or decreased rate of weight gain related with psychostimulants for the treatment of ADHD have not been fully clarified yet. Nesfatin-1, discovered in recent years, released by mainly hypothalamus, is a peptide responsible for the appetite regulation, weight loss and metabolic regulation. We aimed to investigate whether there is an association between nesfatin-1 and etiopathogenesis of ADHD, treatment response and metabolic side effects of MPH by comparing pre-and post-treatment serum levels of Nesfatin- 1 in prepubertal boys with ADHD.
Methods: 33 boys who were diagnosed with ADHD according to DSM IV-TR criterias in Bakirkoy Mental Health Research and Training Hospital, Child and Adolescent Psychiatry outpatient clinic, were included in

the study. All participants were already applied to clinical interview and K-SADS. The appetite level of the patients was evaluated by Turkish version of Children's Eating Behaviour Questionnaire (CEBQ). ADHD symptoms were evaluated by Conners' Teacher and Parent Rating Scale. The patients' nesfatin-1 levels, biochemical metabolic parameters, anthropometric measures were determined before and after MPH treatment.
Results: There was no significant change in serum Nesfatin-1 levels between pre-and post-treatment in the patient group. There were significant decreases in weight, body mass index (BMI), BMI percentile, waist circumferences (WC), WC percentiles of patients after the treatment. There was no significant correlation between Nesfatin-1 levels and BMI, BMI percentile, WC. Food responsiveness and enjoyment of food subscales scores and total scores of CEBQ after the treatment were significantly lower than the pretreatment levels. There was no significant correlation between serum nesfatin- 1 level and the subscales of CEBQ both pre-and post-treatment except for the slowness in eating subscale of CEBQ.
Conclusions: In light of the findings of our study, although MPH associated loss of appetite was observed, there was no clear evidence that this anorexic side effect is through Nesfatin directly. Although the variations in anthropometric body measures after the treatment was observed, there was no clear evidence that these changes could be related to direct effect of Nesfatin

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J Am Acad Child Adolesc Psychiatry. 2016;55:S328-S329.
A NEUROSCIENCE PERSPECTIVE ON THE HETEROGENEITY OF ATTENTION-DEFICIT/ HYPERACTIVITY DISORDER.
Posner J.
Objectives: We will review the neurobiology of ADHD by focusing on neural circuits implicated in the disorder and discuss how abnormalities in circuitry relate to symptom presentation and treatment.
Methods: We will present data from three MRI studies of youth with ADHD. The methods include resting-state functional connectivity MRI (rs-fcMRI), diffusion MRI, and structural MRI.
Results: In study 1, structural and diffusion MRI scans were obtained from 30 children with ADHD and 31 healthy control (HC) subjects (mean age in years 10 ± 2.1 SD). By use of morphometry and probabilistic tractography combined with multivariate statistical modeling, we identified anomalies within the fronto-accumbal circuit in childhood ADHD. The pattern of connectivity was associated with increased aggression (semi-partial correlation = 0.70). In study 2, rs-fcMRI scans were obtained from children with ADHD (n = 22) and without (N = 20) ADHD. We found that children with ADHD had reduced connectivity in two neural circuits: 1) underlying executive attention (EA); and 2) the emotional regulation (ER). We also found double dissociation between these two neural circuits and their behavioral correlates, such that reduced connectivity in the EA circuit correlated with EA deficits ($r = -0.79$, $p < 0.001$), but not with emotional lability ($r = 0.12$, $df = 19$; $p = 0.6$). On the other hand, reduced connectivity in the ER circuit correlated with emotional lability ($r = -0.63$; $p = 0.002$) but not with EA deficits ($r = 0.03$; $p = 0.9$). In study 3, rs-fcMRI scans were obtained from children with ADHD (n = 23) and without (N = 23) ADHD. Graph analysis indicated that connections within the default mode network (DMN) were indicative of delayed maturation on this neural circuit. Of all of the DMN connections quantified, 10 of the 13 connections that typically increase in strength over age were found to be stronger among HC children. In contrast, the one DMN connection known to decrease in strength with age was found to be stronger in the group with ADHD.
Conclusions: ADHD is a heterogeneous disorder, and several neural circuits probably underlie this complex disorder. Novel treatments might use these circuits as targets for treatment development and to aid in developing more personalized interventions

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J Am Acad Child Adolesc Psychiatry. 2016;55:S328.
IMAGING THE SOCIAL CONNECTOME IN CHILDREN WITH ATTENTION-DEFICIT/ HYPERACTIVITY DISORDER AND AUTISM.
DiMartino A.
Objectives: We present initial empirical work examining neural markers of social communicative impairment characteristic of ASD across children with ASD and ADHD. Increasing evidence indicates that autistic traits

(AT) are present in a substantial group of children with ADHD. These children do not meet diagnostic criteria for ASD, present higher functional impairment, or pose a challenge for recognition and treatment. To date, it is unknown whether AT in ADHD and ASD represent similar neurobiological dysfunctions.
Methods: To address this question, we examined resting-state fMRI data from children with ADHD (mean age 9.5 ± 1.6 years), identified as ADHD with AT (ADHD+AT; N = 45), or without ADHD (ADHD-AT; N = 57) per parent responses on the Social Responsiveness Scale. We conducted seed-based connectivity analyses of the right fusiform face area (FFA). After removal of nuisance signals (24-Friston motion parameters, cerebral spinal fluid, and white matter masks), we extracted the residual mean time series for the FFA seed. We then ran between-group analysis using random effect models [covariate: age, motion, subjects, whole-brain intrinsic functional connectivity (iFC) average]. Gaussian random field theory corrected for multiple comparisons ($Z > 2.3$, $p < 0.05$).
Results: Children with ADHD+AT had weaker iFC between the right FFA and left rostral anterior cingulate cortex (ACC). Secondary analyses with agematched children with ASD (N = 57) showed a hypoconnectivity iFC pattern similar to ADHD+AT.
Conclusions: These initial findings highlight a circuit involving two core hubs of the social brain: the FFA subserving face recognition and the ACC subserving ΓÇ£mentalizing.ΓÇØ Weaker iFC between these nodes characterized children with AT regardless of their DSM-based diagnosis, illustrating the use of eschewing extreme comparisons for the identification of potential biomarkers specific to and shared across psychiatric conditions

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J Am Acad Child Adolesc Psychiatry. 2016;55:S222.
DIAGNOSTIC STABILITY AND FUNCTIONAL OUTCOMES OF CHILDREN WITH ATTENTION-DEFICIT/ HYPERACTIVITY DISORDER AT AGE 10 YEARS: A THREE-YEAR CONTROLLED LONGITUDINAL STUDY.
Efron D, Nicholson J, Anderson V, et al.
Objectives: Most longitudinal ADHD studies have examined clinical cohorts, often with a broad age range at baseline precluding the measurement of developmentally sensitive outcomes. This community-based study examined the diagnostic stability and three year outcomes of a sample of children with ADHD and non-ADHD controls recruited at age 7, and investigated differences in outcomes by ADHD persistence and gender.
Methods: Children with ADHD (n=179) and matched non-ADHD controls (n=212) aged 7 were originally recruited through 43 Melbourne schools, using a two-stage screening (parent and teacher Conners 3 ADHD index) and case confirmation (Diagnostic Interview Schedule for Children, Version IV; [DISC-IV]) procedure. Two-thirds in each group were boys. Children were reassessed 3 years later (mean age: 10.5; SD=.5) to examine diagnostic persistence (DISC-IV), mental health disorders (DISC-IV), academic performance (Wide Range Achievement Test 4) and social functioning (parent or teacher reported Peer Problems on Strengths and Difficulties Questionnaire). Linear and logistic regression were used for all analyses.
Results: Sixty-seven percent of children with ADHD continued to meet diagnostic criteria for ADHD three years later. Children with ADHD at age 7 had more externalizing (49 percent vs 10 percent, p<0.001), anxiety (22 percent vs 5 percent, p<0.01) and mood (6 percent vs 0 percent, p=0.03) disorders at follow-up, as well as poorer word reading (mean difference (MD) 10.6; 95% CI 7.4, 13.8; p<0.001), math performance (MD 12.2; 95% CI 9.1, 15.3; p<0.001) and social functioning (71 vs 27 percent; p<.001) compared to non-ADHD controls. Compared to children with remitted ADHD, children with persistent ADHD had increased odds of externalizing disorders (OR 3.5; 95% CI 1.4, 8.6; p=0.007), however had better word reading (MD 5.5; 95% CI 0.2, 10.8; p=.04). Outcomes were similar for boys and girls with ADHD, except that boys were more likely to have persistent ADHD than girls (74 vs 50 percent; p=.01).
Conclusions: One-third of children identified with ADHD at age 7 do not meet ADHD diagnostic criteria three years later. Children with ADHD identified at age 7 have substantially poorer mental health, academic and social outcomes than controls at age 10

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J Am Acad Child Adolesc Psychiatry. 2016;55:S226.

WHAT FACTORS INFLUENCE ATTENTION-DEFICIT/ HYPERACTIVITY DISORDER RATINGS APART FROM ATTENTION-DEFICIT/ HYPERACTIVITY DISORDER TRAITS?

Garcia-Rosales A, Vitoratou S, Chen W.

Objectives: This study aimed to answer the following questions: 1) Are all criteria equally informative in terms of caseness and severity? 2) Are parents and teachers evaluating and assessing the same phenomenon? 3) Is the information provided by different informants influenced by age, gender and comorbidity? 4) Is caseness affected by the different methods of aggregating parent and teacher information?

Methods: 1) The sample was an IMAGE dataset, which is a multi-centered ADHD research project, more specifically parent data from the Parental Account of Clinical Symptoms (PACS) and from teachers (Conners rating scales) and comorbid diagnostic data derived from the Hypescheme. 2) Statistical analyses were carried out using Logistic Regression, Item-Response Theory and Item Factor Analyses.

Results: The sample consisted of 1383 subjects (17.9 percent of females) with ages ranging 4-19 years old. 1) All ADHD criteria contributed significantly and independently to caseness; however, they did not carry equal weighting and provided differential information across the spectrum of latent Inattentiveness (IA) and Hyperactivity/Impulsivity (HI) traits. 2) Parents are better at describing IA and HI across the latent spectrums, whereas teachers are better at differentiating cases from non-cases. 3) Informant characteristics, and the child's age, gender and comorbidity all influence ratings of ADHD symptoms. 4) The rules used to combine parent and teacher information also influence item and information profiles.

Conclusions: The ratings of DSM-5 ADHD criteria are not invariant across informant, and child's gender, age, comorbidity status and aggregation rules used to combine parent and teacher information. There are significant limitations in the current DSM-5 and ICD-10 taxonomic systems

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J Am Acad Child Adolesc Psychiatry. 2016;55:S315.

RELIABILITY AND VALIDITY OF THE BEFORE SCHOOL FUNCTIONING QUESTIONNAIRE IN CHILDREN WITH ATTENTION-DEFICIT/ HYPERACTIVITY DISORDER.

Faraone SV.

Objectives: Children with ADHD frequently manifest behavioral difficulties in the mornings before going to school. We sought to assess the reliability and concurrent validity of the Before School Functioning Questionnaire (BSFQ), which has been proposed as a measure of morning behaviors impaired by the symptoms of ADHD.

Methods: We analyzed BSFQ ratings from a randomized crossover study of subjects ages 6-12 years, comparing the methylphenidate transdermal delivery system (MTS) to a placebo transdermal system (PTS) for a total of 4 weeks. We computed reliability and concurrent validity using pretreatment, baseline assessments on the investigator and child (self)-rated BSFQ, the ADHD Rating Scale, and the Brief Inventory of Executive Functioning (BRIEF).

Results: Our results suggest that the BFSQ investigator-rated scale shows very good internal homogeneity (Cronbach's ± = 0.91), good test-retest reliability (r = 0.60), good concurrent validity (r range 0.42-0.86), and a strong treatment effect (effect size = -0.93). In contrast, the self-rated BSFQ showed lower levels of reliability (± = 0.81), poor test-retest reliability (r = -0.18), no significant evidence of concurrent validity (r range -0.22 to 0.37), and no significant treatment effect (effect size = -0.26).

Conclusions: We suggest that the investigator-rated BSFQ be used in future trials of ADHD medications for youth aimed at assessing efficacy in the morning hours before school. Additional work is needed to further examine the psychometrics of the BSFQ in a normative population and create a reliable and valid self-rated BSFQ

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J Am Acad Child Adolesc Psychiatry. 2016;55:S295.

CLINICAL CORRELATES OF WORKING MEMORY DEFICITS IN YOUTH WITH AND WITHOUT ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.

Fried RS.

Objectives: Both working memory (WM) (the ability to hold information in memory for short periods of time) and ADHD have been associated with educational deficits. Because WM deficits are prevalent in children with ADHD, the main aim of the present study was to examine whether educational deficits are driven by working memory deficits or the effect of ADHD itself.

Methods: Subjects were referred youth with (N = 276) and without (N = 241) ADHD ascertained from pediatric and psychiatric sources. Assessment included measures of psychiatric, psychosocial, educational, and cognitive functioning. Working memory was assessed using the Wechsler Intelligence Scale for Children-Revised Freedom from Distractibility (FFD) factor based on digit span, arithmetic, and coding. We classified subjects as having WM deficits if they had a significant difference between their IQ and the FFD factor or if they had a SD of 1.5 below average FFD factor. We chose the FFD subscale because it is highly correlated with the present Wechsler measure of WM.

Results: Significantly more youth with ADHD had WM deficits than control subjects (31.9 vs. 13.7 percent, $P < 0.05$), and in ADHD children, their presence was significantly ($P < 0.01$) associated with an increased risk for grade retention and placement in special classes and lower scores on reading and math achievement tests, relative to ADHD subjects without WM deficits. In contrast, no other differences were noted in other areas of functioning. Although WM deficits also had some adverse impact on educational and cognitive correlates in non-ADHD control subjects, these differences failed to attain statistical significance.

Conclusions: WM deficits significantly and selectively increase the risk for academic deficits and cognitive dysfunction in children with ADHD beyond those conferred by ADHD. Screening for WM deficits may help identify children with ADHD at high risk for academic and cognitive dysfunction

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J Am Acad Child Adolesc Psychiatry. 2016;55:S166.

MANAGEMENT OF ATTENTION-DEFICIT/ HYPERACTIVITY DISORDER IN PRIMARY CARE: DO PRACTICES DIFFER FOLLOWING SHORT-TERM PSYCHIATRIC TREATMENT?

Rockhill CM, Carlisle L, Stoep AV, et al.

Objectives: This study uses data from the Children's ADHD Telemental Health Treatment Study (CATTS), an NIMH-funded effectiveness trial. Subjects had ADHD with or without comorbid ODD or anxiety and were randomized to one of two treatment group: group A-CATTS intervention with six sessions of telepsychiatry and parent behavioral management; or group B- treatment by PCPs augmented by a single telepsychiatry consultation. Children in both groups improved over 22 weeks, but those in the CATTS intervention had greater improvement in ADHD, ODD, and functioning. Here, we examine whether study condition during the trial influenced subsequent management at 32 weeks of ADHD for children in group A vs. group B and adherence to the telepsychiatrists' recommendations.

Methods: Of the 223 subjects participating in the CATTS trial, we were able to obtain follow-up records for 200 subjects, with no difference in participation between groups. We used t-tests and ANOVA to compare follow-up visits, use of medication, categories of medication, and PCPs' adherence to telepsychiatrists' recommendations. In addition, we examined the effects of comorbidity on PCPs' management, controlling for group assignment.

Results: Children in the CATTS intervention group were more assertively managed during short-term follow-up than those assigned to the augmented PCP group as evidenced by greater mean number of follow-up visits from 22 to 32 weeks (2.1 vs. 0.7, $P < 0.001$), greater likelihood of taking ADHD medications at follow-up ($t = 2.76$, $P < 0.001$), and higher doses of stimulant medications ($P < 0.05$). We found that the presence of comorbidity was associated with polypharmacy ($P < 0.05$) in both groups and that youth with higher symptom severity had more follow-up sessions with PCPs at 32 weeks for group A but not for group B. PCPs were more likely to be adherent to medication treatment recommendations made by the telepsychiatrist in the intervention condition ($t = 4.32$, $P < 0.01$).

Conclusions: These findings suggest that short-term interventions for ADHD provided by child and adolescent psychiatrists are more effective in influencing PCPs' subsequent management of ADHD than a

single consultation session. They also suggest ongoing roles for psychiatry in helping our primary care colleagues to more assertively pursue treatment to optimal symptom remission

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J Am Acad Child Adolesc Psychiatry. 2016;55:S215.

EARLY CLINICAL INDICATORS OF PERSISTENT ATTENTION-DEFICIT/HYPERACTIVITY DISORDER IN LOW BIRTH WEIGHT/PRETERM SURVIVORS.

Stratigos K, Turner JB, Feldman JF, et al.

Objectives: Previous research on a prospective cohort of preterm infants with low birth weight identified three latent classes based on longitudinal patterns of ADHD symptoms. One class had persistent inattention problems through adolescence but differed slightly from the other classes in terms of ADHD presentation at age 6 years. This study attempts to identify characteristics that might distinguish children likely to have chronic inattention problems from those whose symptoms are considered minor or transitory.

Methods: The Neonatal Brain Hemorrhage Study (NBHS) followed a cohort of infants with low birth weight who were born in the years 1984 through 1987 in three New Jersey counties. Psychiatric assessments using the DISC were made at three ages: 6, 9, and 16 years. This session focuses on the subset of subjects who completed these assessments at all three waves (n = 387).

Results: A number of variables of inattention in patients at age 6 years, readily discernible in the office setting, predicted clinically relevant inattention at age 16 years. These included nocturnal enuresis, motor problems, cerebral palsy, inadequate social skills, and aggressive behaviors. The risks for chronic inattention problems imposed by many of these factors were overlapping so that only a subset was necessary to comprise an effective indicator. An indicator defined as the presence of least two symptoms of inattention of age 6 years plus any one of either nocturnal enuresis, inadequate social skills, or cerebral palsy captured approximately 25 percent of the subjects with clinically relevant inattention problems at age 16 years (defined as four or more DSM-IV inattention criteria plus impairment). The rate of false positives is modest (specificity = 0.96, PPV = 0.69). When DSM-IV ADHD (predominantly inattentive and combined types) at age 16 years is used as the standard, sensitivity is improved with commensurate declines in specificity and positive predictive value (PPV) (sensitivity = 0.34, specificity = 0.94, PPV = 0.43).

Conclusions: Early inattention symptoms can be used as a predictor of chronic problems when these symptoms are accompanied by one or more of the following indicators: nocturnal enuresis, inadequate social skills, and/or cerebral palsy. Children with early inattention and one or more of these risk factors would be well served by close monitoring and, potentially, a plan for early intervention and treatment

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J Am Acad Child Adolesc Psychiatry. 2016;55:S112-S113.

DSM-IV AND DSM-5 ATTENTION-DEFICIT/ HYPERACTIVITY DISORDER PREVALENCE AMONG 12-YEAR-OLD STUDENTS IN BRAZIL: CONTEXTUAL FACTORS AND COMORBID PATTERNS.

Ribeiro MVV, Sanudo A, Fidalgo TM, et al .

Objectives: ADHD is the most prevalent youth psychiatric disorder. It is highly comorbid with internalizing [generalized anxiety disorder (GAD), PTSD, MDD] and externalizing disorders (ODD, CD). The new edition of DSM-5 presents modified diagnostic criteria compared with the old version (DSM-IV). Our aim was to measure the prevalence of ADHD and comorbid psychiatric disorders according to DSM-IV and DSM-5.

Methods: Data came from an epidemiological study, including 180 students (ages 12 years) in nine public schools from two S+úo Paulo city neighborhoods. Psychopathology was assessed by the KSADS and Schizophrenia for School- Age Children-Present and Lifetime Version. Data were analyzed using weighted logistic regression.

Results: Weighted ADHD prevalence was 9.4 percent (DSM-IV) and 13.3 percent (DSM-5). Inattention subtype comprised most of the new cases diagnosed by means of DSM-5 (72.7 percent; P = 0.287). In a multivariate model, low SES, GAD4, and MDD4 were associated significantly with ADHD4 (OR = 4.76; P = 0.009; OR = 4.20; P = 0.025; OR = 3.99; P = 0.017, respectively). Male gender, low SES, GAD5, and MDD5

were associated significantly with ADHD5 (OR = 3.63; P = 0.002; OR = 3.01; P = 0.015; OR = 7.73; P = 0.005; OR = 5.88; P = 0.003, respectively).
Conclusions: Most new cases diagnosed by means of DSM-5 criteria undiagnosed by DSM-IV were of the inattentive subtype. ADHD in youth in S+úo Paulo is highly comorbid with anxiety and mood disorders and DSM-5 identified several cases not identified by DSM-IV

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J Am Acad Child Adolesc Psychiatry. 2016;55:S314-S315.
EARLY MORNING FUNCTIONING IN ATTENTION-DEFICIT/HYPERACTIVITY DISORDER: BACKGROUND AND IMPACT.
Sallee FR.
Objectives: Despite improvements with drug delivery systems of the ADHD medications, early morning functioning (EMF) remains an issue in many school-age children with ADHD. The most commonly prescribed long-acting stimulants can leave up to 2 hours of the early morning routine (EMR) with inadequately controlled ADHD symptoms. This discussion will review information regarding a recent survey designed to examine the temporal occurrence and severity of inadequate ADHD symptom control and related functional impairments throughout the day in school-age children with ADHD who are currently treated with stimulant medications and the impact on caregivers.
Methods: An online primary caregiver-completed questionnaire (n = 201) was designed to determine whether inadequately controlled ADHD symptoms exist in school-age children with ADHD who currently are treated with stimulants. Caregivers who identified controlled ADHD symptoms inadequately during the EMR (Likert severity rating >2) were asked to continue the survey by answering a series of questions.
Results: In a recent survey, inadequately controlled ADHD symptoms were rated as most severe during the early morning routine (6.45) and the evening homework time (6.46) on a 10-point scale (1 = no ADHD symptoms and 10 = significant ADHD symptoms). Majorities of caregivers reported early morning ADHD symptoms (74 percent) and impairment of early morning functioning (EMF) (76 percent) as moderate to severe (ADHD symptom score 5-10). Parents reported that they often felt overwhelmed and exhausted (41 percent), raised their voice more (37 percent), and felt constantly stressed (30 percent) as a result of their child's ADHD symptoms during the EMR. Furthermore, almost half of all caregivers surveyed have woken up early to administer ADHD medication. In addition, 79 percent of caregivers have discussed early morning impairment with their doctor. The most common early morning ADHD symptoms reported are that children are distracted easily, do not listen well, and are unable to sustain attention to tasks.
Conclusions: Despite early morning administration of stimulants, caregivers of school-age children with ADHD report a high prevalence of inadequately controlled, early morning ADHD symptoms, which has a negative impact on caregivers

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J Am Acad Child Adolesc Psychiatry. 2016;55:S281-S282.
FROM COMMUNITY TO CLINIC AND BACK: WHAT POPULATION-BASED SAMPLES CAN TELL US ABOUT THE GENETICS OF PSYCHOPATHOLOGY IN YOUTH.
Schachar RJ, Willcutt EG.
Objectives: Population-based sample groups provide a novel opportunity to elucidate the etiology of psychiatric disorders. These large sample groups with phenotypic, genetic, and often environmental data can provide the statistical power needed to identify genetic variants involved in psychiatric disorders and determine how genetic risk can modulate the effects of environmental risk on brain and behavior. Our symposium showcases the power of population-based approaches to help uncover the biological mechanisms of psychiatric traits.
Methods: In study 1, the Spit for Science (SfS) sample group used a novel hypothesis- driven genome-wide association study (GWAS) to examine the role of neurodevelopment genetic variants in obsessive-compulsive traits in approximately 5,300 children and adolescents of European ancestry. Study 2 also used the SfS sample group and hypothesis-driven GWAS approach but examined a neurocognitive endophenotype for ADHD, response inhibition as measured by performance on the Stop-Signal Task. Study

3 combined three population-based sample groups [the Saguenay Youth Study, the IMAGEN study, and the Avon Longitudinal Study of Parents and Children (ALSPAC)] to examine whether polygenic risk for schizophreniamoderated the relationship between adolescent cannabis use and cortical thickness in a sex-dependent way. Finally, study 4 examined the possible interactions among birth weight, maternal sensitivity, and dopaminergic risk variants on a later attachment in 590mother-child dyads from the MAVAN (Maternal Adversity, Vulnerability and Neurodevelopment) Cohort.
Results: In the SfS sample group, hypothesis-driven methods identified genome-wide significant hits in PTPRD and NPAS2 associated with obsessivecompulsive traits and the collective role of genetic variants involved in brain development in both obsessive-compulsive traits and response inhibition. Study 3 showed that adolescent cannabis use was associated with reduced cortical thickness, but only in males with high polygenic risk for schizophrenia. The MAVAN study found that dopaminergic risk variants interacted with birth weight and maternal sensitivity to predict disorganized attachment.
Conclusions: Our results provide insights into the possible etiological factorszs that contribute to various psychiatric conditions and demonstrate the feasibility and power of population-based approaches to psychiatric research

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J Am Acad Child Adolesc Psychiatry. 2016;55:S234.

PSYCHOTIC RISK SYMPTOMS AND POTENTIAL TRAUMATIC EVENTS AMONG ADOLESCENTS WITH AUTISM SPECTRUM DISORDERS OR ATTENTION-DEFICIT/ HYPERACTIVITY DISORDER.

Unenge Hallerb+ñck M, Habul N, Hj+ñrthag F, et al.

Objectives: The aim was to investigate the amount of psychotic risk symptoms and potential traumatic events among adolescents with ASD and/ or ADHD.
Methods: Data comes from a Swedish cohort study of 85 patients (48 with ASD and 37 with ADHD), aged 16-18 years, collected at a Child and Adolescent Psychiatry (CAP) clinic. Two self-report instruments were used to measure psychotic risk symptoms, the Youth Psychosis At Risk Questionnaire- Brief Version (YPARQ-B) and the Prodromal Questionnaire- Brief Version (PQB). To evaluate traumatic experiences, Link+Âping Youth Life Experience Scale (LYLES), was used. The YPARQ-B consists of 28 items and a total score above 11 indicates an increased risk for psychosis. The PQ-B consists of 21 items and cut-off values of 3 and 6 were used.
Results: A majority of the participants reported having experienced at least one psychotic symptom (68.2 percent on YPARQ-B and 87.1 percent on PQB), median on YPARQ-B was 3.0 (Range 0 to 18) and median on PQ-B was 5.0 (Range 0 to 17). Seven individuals had a value above the YPARQ-B cut-off value, and 63 individuals scored above 3 on PQ-B, while 34 individuals scored 6 or higher on PQ-B. When comparing the ASD and ADHD groups on YPARQB and PQ-B (Mann-Whitney U tests), no significant difference between the groups was found on YPARQ-B. For PQ-B, the participants in the ASD-group reported a higher amount ($p=0.034$) of psychotic risk symptoms (Md = 5.0) than those in the ADHD-group (Md = 3.0). The correlation (Spearman's rho) between YPARQ-B and potential traumatic events (LYLES) was medium strong ($rho= 0.428$, $p< 0.001$) as was the correlation between PQ-B and LYLES ($rho= 0.448$, $p< 0.001$).
Conclusions: We concluded that psychotic risk symptoms are frequent in both groups studied, but more common in the ASD-group according to the PQ-B questionnaire. Also, there were significant associations between psychotic risk symptoms and potential traumatic events. Altogether our results suggest that the overlap between neurodevelopmental disorders, an increased risk for psychosis, and potential influence of traumatic events ought to be considered in future research

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J Am Acad Child Adolesc Psychiatry. 2016;55:S207.

EFFECT OF ADENOTONSILLECTOMY ON ATTENTION-DEFICIT/HYPERACTIVITY DISORDER SYMPTOMS, SLEEP DISTURBANCE SYMPTOMS, AND QUALITY OF LIFE OF CHILDREN WITH ADENOTONSILLAR HYPERTROPHY AND SLEEPDISORDERED BREATHING.

Turkoglu S, Somuk BT, Sapmaz E, et al.

Objectives: Chronic adenotonsillar hypertrophy is the most common etiologic cause for the obstruction of the upper airways in childhood and has been found to be related with a variety of psychiatric problems and poor quality of life. To date, limited data has been available regarding the impact of adenotonsillectomy (AT) on the psychosocial well-being of chronic adenotonsillar hypertrophy subjects. In the present study, we examined the impacts of AT on ADHD and sleep disturbance symptoms and quality of life of children with chronic adenotonsillar hypertrophy.

Methods: Parents of children with chronic adenotonsillar hypertrophy filled in Conners Parent Rating Scale-Revised Short (CPRS-RS), Children's Sleep Habits Questionnaire (CSHQ), and The Pediatric Quality of Life Inventory, Parent versions (PedsQL-P) before and six months after AT. Paired t-test was used to test for mean differences between these ratings.

Results: A total of 64 children were included the study (mean age, 6.8 ± 2,4, years; 50% boys). Mean ADHD Index (11.98 ± 6.94 versus 10.35 ± 6.44) (before AT versus after AT) and oppositional scores (6.73 ± 3.72 versus 5.87 ± 3.52) improved statistically significantly after AT ($p < 0.05$). Cognitive problems /inattention and hyperactivity scores was reduced, but were not statistically significant ($p > 0.05$). All of the CSHQ subdomain scores (bedtime resistance, sleep-onset delay, sleep anxiety, night waking, parasomnias, sleep disordered breathing, daytime sleepiness), except sleep duration, significantly reduced after AT ($p < 0.05$). Regarding to quality of life, both PedsQL-P physical health (64.20±19.81 versus 69.84±18.63) and psychosocial health subdomain scores (67,83±12.89 versus 75.57±13.16), and PedsQL-P total score (66.57±12.94 versus 73.58±12.46) of the patients were significantly higher six months after AT ($p < 0.001$).

Conclusions: It is necessary for child and adolescent psychiatrists to query the symptoms of chronic adenotonsillar hypertrophy to identify children with chronic adenotonsillar hypertrophy who suffer from ADHD symptoms, oppositionality, and sleep disturbance. To carry out AT seems to be beneficial for coexisting ADHD and sleep disorder symptoms and quality of life in these children

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J Am Acad Child Adolesc Psychiatry. 2016;55:S127.

THE ABNORMAL REGIONAL NEURAL FUNCTION AND FUNCTIONAL INTEGRATION OF THE CEREBELLUM IN CHILDREN AND ADOLESCENTS WITH ATTENTION-DEFICIT/ HYPERACTIVITY DISORDER.

Mizuno Y, Jung M, Fujisawa T, et al.

Objectives: Impaired executive function is one of the most widespread conceptual factors in ADHD. The cerebellum, traditionally considered a motor structure, has been increasingly recognized as an important structure in cognitive function, including executive function. The aim of the present study is to elucidate whether the region and network of the cerebellum involved in executive function are different in children and adolescents with ADHD compared with healthy control subjects.

Methods: Thirty-two patients with ADHD (ages 7-13 years) and 31 age- and IQ-matched healthy control subjects (ages 7-14 years) underwent imaging by using resting-state (rs)-fMRI). An amplitude of low-frequency fluctuation (ALFF), which is the index of regional spontaneous brain activity and functional connectivity (FC) of crus I/II in the cerebellum, was analyzed. This study was approved by the ethics committee at the University of Fukui, and written informed consent was obtained from all participants and parents.

Results: Relative to healthy control subjects, patients with ADHD showed significantly higher ALFF in left lobule VI, crus I, right lobule VIII, and crus I/II in the cerebellum, and significantly less FCs of left crus I/II with anterior cingulate cortex (ACC), bilateral dorsolateral prefrontal cortex (DLPFC), and right inferior parietal lobule (IPL) and less FCs of right crus I/II with right DLPFC and IPL. In addition, across patients with ADHD, ALFF in left crus I and FC of left crus I/II with ACC were correlated significantly with ADHD-rating scale IV total score ($r = 0.39$, $P = 0.03$; $r = -0.40$, $P = 0.02$, respectively). Further, FC of left crus I/II with ACC also was correlated significantly with a performance of working memory in Wechsler Intelligence Scale for Children-Fourth Edition ($r = 0.49$, $P < 0.01$).

Conclusions: These results suggest that altered regional neural activity and cortico-cerebellar circuit, including crus I/II, are involved in the pathology of ADHD, especially executive function, such as working memory, which might lead to the development of a biomarker that would evaluate ADHD objectively

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J Am Acad Child Adolesc Psychiatry. 2016;55:S168.

HEART FAILURE AND CARDIOMYOPATHY FOLLOWING INITIATION OF MEDICATIONS FOR ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.

Mosholder AD, Taylor L, Mannheim G, et al.

Objectives: The goal of this presentation is to assess the incidence of heart failure and cardiomyopathy in pediatric and adult stimulant users without prior history of heart failure by duration of stimulant use. Stimulant abuse can be associated with cardiomyopathy, but little is known about cardiomyopathy with long-term therapeutic stimulant use.

Methods: Data were obtained from 15 data partners contributing their administrative claims or electronic health record information through the Sentinel Distributed Database. Age-groups were <22, 22-44, 45-64, and 65+ years, and ADHD medications included were amphetamine products (including lisdexamfetamine), methylphenidate, and atomoxetine. Patients were excluded if they had an ADHD medication or if there was an outcome in the 183 days before exposure. Exposure was considered continuous if gaps in a day's supply were <90 days. Only each patient's first exposure was included. The outcome was considered a heart failure or cardiomyopathy according to the ICD-9-Clinical Modification diagnosis codes (398.91, 402.x1, 402.x3, 404.x1, 404.x3, 422.90, 425.4, 425.9, 428.xx) in any care setting (but had to be a principal diagnosis in an inpatient or institutionalized care). We analyzed the incidence of the outcome during the following specific periods of continuous use: 0-90, 91-180, 181-270, 271-365, 366-730, and 731-1,095 days.

Results: Our sample group included 2,062,725 ADHD medication users of all ages, of whom 44.6 percent were female and 53.9 percent were under age 22 years. In patients age <22 years, heart failure outcome rates for amphetamine and methylphenidate ranged from 10 to 20 per 10,000 person-years, with no clear trend for increased rates with longer use. Outcome rates in patients age <22 years with atomoxetine ranged from 4 to 44 per 10,000 person-years, again with no clear trend for higher rates with longer use. Heart failure rates increased with age, with the highest rates in the age category of 65+ years. In the older age-groups, higher rates occurred earlier during treatment.

Conclusions: Heart failure rates did not increase over 3 years of use of ADHD medications. In older age-groups, lower heart failure rates later in treatment could reflect depletion of susceptibles if patients at risk of developing heart failure with the medication do so earlier in the course of treatment. Labels for all three medication types caution against use in patients with cardiovascular disease

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J Am Acad Child Adolesc Psychiatry. 2017;56:40-50.

ASSOCIATION OF PRETERM BIRTH WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER□LIKE AND WIDER-RANGING NEUROPHYSIOLOGICAL IMPAIRMENTS OF ATTENTION AND INHIBITION.

Rommel AS, James SN, McLoughlin G, et al.

Objective Preterm birth has been associated with an increased risk of attention-deficit/hyperactivity disorder (ADHD)ΓÇôlike symptoms and cognitive impairments similar to those seen in ADHD, including attention and inhibitory control difficulties. Yet data on direct comparisons across ADHD and preterm birth on cognitive-neurophysiological measures are limited.

Method We directly compared 186 preterm-born adolescents to 69 term-born adolescents with ADHD and 135 term-born controls on cognitive-performance and event-related potential measures associated with attentional and inhibitory processing from a cued continuous performance test (CPT-OX), which we have previously shown to discriminate between the adolescents with ADHD and controls. We aimed to elucidate whether the ADHD-like symptoms and cognitive impairments in preterm-born individuals reflect identical cognitive-neurophysiological impairments in term-born individuals with ADHD.

Results Go-P3 amplitude was reduced, reflecting impaired executive response control, in preterm-born adolescents compared to both controls and adolescents with ADHD. Moreover, in preterm-born adolescents, as in term-born adolescents with ADHD, contingent negative variation amplitude was attenuated, reflecting impairments in response preparation compared to controls. Although the ADHD group showed significantly increased NoGo-P3 amplitude at FCz compared to preterm group, at Cz preterm-born adolescents demonstrated significantly decreased NoGo-P3 amplitude compared to the control group, similar to term-born adolescents with ADHD.
Conclusion These findings indicate impairments in response preparation, executive response control, and response inhibition in preterm-born adolescents. Although the response preparation and response inhibition impairments found in preterm-born adolescents overlap with those found in term-born adolescents with ADHD, the preterm group also shows unique impairments, suggesting more wide-ranging impairments in the preterm group compared to the ADHD group

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J Am Acad Child Adolesc Psychiatry. 2017;56:167-74.
THE FAMILIAL CO-AGGREGATION OF ATTENTION-DEFICIT/HYPERACTIVITY DISORDER AND INTELLECTUAL DISABILITY: A REGISTER-BASED FAMILY-ÁSTUDY.
Faraone SV, Ghirardi L, Kuja-Halkola R, et al.
Objective Although many studies document an association between attention-deficit/hyperactivity disorder (ADHD) and intellectual disability (ID), little is known about the etiology of this comorbidity and how it should be addressed in clinical settings. We sought to clarify this issue.
Method All individuals born in Sweden between 1987 and 2006 (n-á= 2,049,587) were identified using the Medical Birth Register (MBR). From this we selected 7 cohorts of relatives: 1,899,654 parent' offspring pairs, 4,180 monozygotic twin pairs, 12,655 dizygotic twin pairs, 914,848 full sibling pairs, 136,962 maternal half-sibling pairs, 134,502 paternal half-sibling pairs, and 2,790,164 full cousin pairs. We used within-individual and within-family analyses to assess the association between ADHD and ID.
Results Individuals with ID were at increased risk for ADHD compared to those without ID, and relatives of participants with ID were at increased risk of ADHD compared with relatives of those without ID. The magnitude of this association was positively associated with the fraction of the genome shared by the relative pair and was lower for severe compared with mild and moderate ID. Model-fitting analyses demonstrated that 91% of the correlation between the liabilities of ADHD and ID was attributable to genetic factors.
Conclusion These data provide evidence that nearly all of the comorbidity between ADHD and ID can be attributed to genetic factors, which has implications for diagnostic practice

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Kennedy Inst Ethics J. 2016;26:249-75.
TRANSCULTURAL ADHD AND BIOETHICS: REFORMULATING A DOUBLY DICHOTOMIZED DEBATE.
Pickering N, Nie JB.
A double dichotomization, of biology and culture, and of cultures (the difference presumption), is to be found in debates about Attention Deficit Hyperactivity Disorder (ADHD) in cross-cultural psychiatric and bioethics literature. The double dichotomy takes biology to explain cross-cultural similarities and culture to explain inter-cultural differences. In this paper, the double dichotomy is explored in debates on the significance of the worldwide prevalence of ADHD, and on the cogency of cross-cultural diagnosis of ADHD in the central character of Chinese classic novel The Dream of the Red Chamber. Contrary to the difference presumption, cultures are not homogenous unities that contrast in toto with one another. The Dream reveals parallels to contemporary US debates-the medicalization of human life and normative disputes about childhood behaviors. To overcome the empirical and theoretical shortcomings of the difference presumption and its underlying characterization of cultural differences, a transcultural approach is proposed and its potential advantages illustrated

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Matern Child Health J. 2016 Apr;20:915-24.

PARENT-REPORTED HEALTH CONSEQUENCES AND RELATIONSHIP TO EXPENDITURES IN CHILDREN WITH ADHD.

deJong NA, Williams CS, Thomas KC.

OBJECTIVES: (1) To describe parents' report of special needs for children with ADHD on the Children with Special Health Care Needs (CSHCN) Screener; and (2) to assess the association between responses to Screener items and annual mental health and total health expenditures per child.

METHODS: In pooled 2002-2011 Medical Expenditure Panel Survey (MEPS) data, we identify children ages 4-17 years with ADHD. We use OLS and two-part regressions to model the relationship between CSHCN Screener items and mental health and total health expenditures. Based on these models we estimate adjusted, average total health expenditures for children with ADHD-both with and without a co-morbid mental health condition-and different combinations of endorsed Screener items. This research was conducted in accordance with prevailing ethical principles.

RESULTS: There were 3883 observations on 2591 children with ADHD. Without a co-morbid mental health condition, average total expenditures per year from adjusted, model-based estimates were $865 for those meeting no Screener items, $2664 for those meeting only the medication item, $3595 for those meeting the medication and counseling items, and $4203 for those meeting the medication, counseling, and use of more health services items. Children with a co-morbid mental health condition had greater total health expenditures for each combination of Screener items. The associations between Screener items and mental health expenditures were similar, but with a slightly lower marginal effect of the medication item ($p < 0.001$ for all comparisons).

CONCLUSIONS: Parents' responses on the CSHCN Screener are associated with meaningful variation in expenditures for children with ADHD. Though cross-sectional, this study suggests that the CSHCN Screener can be a useful categorization scheme for children with ADHD. It may be an efficient, standardized tool at the point of care for identifying children who need more resources and for targeting intensive interventions in the context of population health management

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Meta Gene. 2017;11:117-22.

FUNCTIONAL GENETIC POLYMORPHISMS IN DOPAMINERGIC TRANSPORTERS: ASSOCIATION WITH ADHD TRAITS IN THE INDIAN PROBANDS.

Ghosh P, Maitra S, Saha T, et al.

Objectives The dopamine (DAT) and norepinephrine (NET) transporters, encoded by SLC6A3 and SLC6A2 genes, regulate neurotransmitters controlling motor activity, attention, mood swings, and stress induced anxiety, thus becoming targets for therapeutic intervention. We explored contribution of SLC6A3 (rs40184, rs2652511) and SLC6A2 (rs3785143, rs11568324) variants in Attention-deficit hyperactivity disorder associated traits.

Methods Nuclear families with ADHD probands (N-á=-á200) and ethnically matched controls (N-á=-á180) were recruited based on the DSM-IV-TR. Behavioral traits were assessed by the Conners' Parent Rating Scale-revised. Genomic DNA obtained from peripheral blood leukocytes was subjected to PCR based amplification of target sites followed by restriction fragment length polymorphism and sequencing based analysis. Statistical analysis was performed by population as well as family-based methods.

Results The control population showed significant difference in allelic and genotypic frequencies for rs40184, rs2652511 and rs11568324 in comparison to other Asian populations. Family-based analysis exhibited preferential transmission of rs3785143 and rs11568324 alleles (P-á=-á0.009 & 0.05). Gene variants showed association with behavioral problems and co-morbid disorders. Multifactor Dimensionality Reduction analysis revealed independent as well as synergistic effects of studied sites and phenotypic traits.

Conclusion Data obtained for the first time evidenced association of dopamine and norepinephrine transporter gene variants with phenotypic traits and co-morbidity of Indian ADHD probands

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MMWR Morb Mortal Wkly Rep. 2016 May;65:443-50.

VITAL SIGNS: NATIONAL AND STATE-SPECIFIC PATTERNS OF ATTENTION DEFICIT/HYPERACTIVITY DISORDER TREATMENT AMONG INSURED CHILDREN AGED 2-5 YEARS - UNITED STATES, 2008-2014.

Visser SN, Danielson ML, Wolraich ML, et al.

BACKGROUND: Attention deficit/hyperactivity disorder (ADHD) is associated with adverse outcomes and elevated societal costs. The American Academy of Pediatrics (AAP) 2011 guidelines recommend "behavior therapy" over medication as first-line treatment for children aged 4-5 years with ADHD; these recommendations are consistent with current guidelines from the American Academy of Child and Adolescent Psychiatry for younger children. CDC analyzed claims data to assess national and state-level ADHD treatment patterns among young children.

METHODS: CDC compared Medicaid and employer-sponsored insurance (ESI) claims for "psychological services" (the procedure code category that includes behavior therapy) and ADHD medication among children aged 2-5 years receiving clinical care for ADHD, using the MarketScan commercial database (2008-2014) and Medicaid (2008-2011) data. Among children with ESI, ADHD indicators were compared during periods preceding and following the 2011 AAP guidelines.

RESULTS: In both Medicaid and ESI populations, the percentage of children aged 2-5 years receiving clinical care for ADHD increased over time; however, during 2008-2011, the percentage of Medicaid beneficiaries receiving clinical care was double that of ESI beneficiaries. Although state percentages varied, overall nationally no more than 55% of children with ADHD received psychological services annually, regardless of insurance type, whereas approximately three fourths received medication. Among children with ESI, the percentage receiving psychological services following release of the guidelines decreased significantly by 5%, from 44% in 2011 to 42% in 2014; the change in medication treatment rates (77% in 2011 compared with 76% in 2014) was not significant.

CONCLUSIONS AND COMMENTS: Among insured children aged 2-5 years receiving clinical care for ADHD, medication treatment was more common than receipt of recommended first-line treatment with psychological services. Among children with ADHD who had ESI, receipt of psychological services did not increase after release of the 2011 guidelines. Scaling up evidence-based behavior therapy might lead to increased delivery of effective ADHD management without the side effects of ADHD medications

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NeuroImage. 2017;144:275-86.

THE NEURO BUREAU ADHD-200 PREPROCESSED REPOSITORY.

Bellec P, Chu C, Chouinard-Decorte F, et al.

In 2011, the ADHD-200 Global CompetitionΓÇØ was held with the aim of identifying biomarkers of attention-deficit/hyperactivity disorder from resting-state functional magnetic resonance imaging (rs-fMRI) and structural MRI (s-MRI) data collected on 973 individuals. Statisticians and computer scientists were potentially the most qualified for the machine learning aspect of the competition, but generally lacked the specialized skills to implement the necessary steps of data preparation for rs-fMRI. Realizing this barrier to entry, the Neuro Bureau prospectively collaborated with all competitors by preprocessing the data and sharing these results at the Neuroimaging Informatics Tools and Resources Clearinghouse (NITRC) (http://www.nitrc.org/frs/?group_id=383). This ADHD-200 Preprocessed release included multiple analytical pipelines to cater to different philosophies of data analysis. The processed derivatives included denoised and registered 4D fMRI volumes, regional time series extracted from brain parcellations, maps of 10 intrinsic connectivity networks, fractional amplitude of low frequency fluctuation, and regional homogeneity, along with grey matter density maps. The data was used by several teams who competed in the ADHD-200 Global Competition, including the winning entry by a group of biostaticians. To the best of our knowledge, the ADHD-200 Preprocessed release was the first large public resource of preprocessed resting-state fMRI and structural MRI data, and remains to this day the only resource featuring a battery of alternative processing paths

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NeuroImage Clin. 2017;13:123-29.

THE AGE-DEPENDENT EFFECTS OF A SINGLE-DOSE METHYLPHENIDATE CHALLENGE ON CEREBRAL PERFUSION IN PATIENTS WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.

Schrantee A, Mutsaerts HJMM, Bouziane C, et al.

Methylphenidate (MPH) is a stimulant drug and an effective treatment for attention-deficit/hyperactivity disorder (ADHD) in both children and adults. Pre-clinical studies suggest that the response to stimulants is dependent on age, which may reflect the ontogeny of the dopamine (DA) system, which continues to develop throughout childhood and adolescence. Therefore, the aim of this study was to investigate the modulating effect of age on the cerebral blood flow (CBF) response to MPH in stimulant treatment-naive children and adults with ADHD. Ninety-eight stimulant treatment-naive male pediatric (10ΓÇô12-áyears) and adult (23 - years) patients with ADHD were included in this study. The CBF response to an acute challenge with MPH (0.5-ámg/kg) was measured using arterial spin labeling (ASL) pharmacological magnetic resonance imaging, as a proxy for DA function. Region-of-interest (ROI) analyses were carried out for the striatum, thalamus and medial prefrontal cortex and in addition voxel-wise analyses were conducted. An acute challenge with MPH decreased CBF in both children and adults in cortical areas, although to a greater extent in adults. In contrast, ROI analyses showed that MPH decreased thalamic CBF only in children, but not adults. Our findings highlight the importance of taking the developmental perspective into account when studying the effects of stimulants in ADHD patients

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Neuropsychopharmacology. 2016;41:S54-S55.

SEROTONERGIC FUNCTION AND EARLY ADULTHOOD OUTCOMES IN CHILDREN WITH DISRUPTIVE BEHAVIOR DISORDERS.

Ivanov I.

Background: The relations between abnormal serotonergic function and impulsive aggression has been studied in both animal and human research. Decreased serotonergic function has been demonstrated in individuals with borderline and antisocial personality disorders (ASPD), intermittent explosive disorder, and impulsive individuals with substance use disorders. Thus serotonergic abnormalities have been associated with both categorical (e.g. personality disorder diagnoses) and dimensional (e.g. aggression, impulsivity, hostility) features of adult psychopathology. For this report we evaluated the longitudinal relations between serotonergic functions in clinically referred children ages 7-11 diagnosed with ADHD and clinical outcomes (e.g. ADHD/ASPD diagnoses and symptoms) in early adulthood.

Methods: Our group has conducted a longitudinal follow up of an ethnically diverse cohort of children with ADHD (n = 155) who had two waves of follow up assessments. The sample was initially recruited between 1990 and 1997 when the participants were aged 7-11 years; all participants completed a comprehensive clinical evaluation and a subgroup of 110 also completed a fenfluramine challenge test. Measures of prolactin levels and vital signs (heart rate, blood pressure) were obtained at baseline, 60min, 120min, 180min, 240min and 300min. The second wave assessment included interviews from participant and informant (e.g. parent) for the identification of Axis II psychopathology. A third wave follow-up was conducted between 2006-2011 (average 15 years after the baseline assessment) including interviews with participants to identify adult Axis I and Axis II psychopathology. Of the participants who presented for the third assessment we analyzed 40 adults who completed the fenfluramine challenge procedure in childhood.

Results: Twenty-one participants (52.5%) met criteria for ASPD; of these 11 participants were diagnosed with ASPD during the second follow up and had the diagnosis confirmed at the third follow up. Additional 10 participants were newly diagnosed with ASPD for the first time as adults. All participants who were diagnosed with ASPD had received an CD diagnosis in childhood. Step-wise logistic regression analyses with ASPD as dependent variable show that childhood CD predicted independently ASPD (p =.020) where childhood socio-economic status (SES) was not a significant predictor. Repeated measures ANOVA showed distinct patterns for prolactin response for participants with ASPD vs. no-ASPD. Specifically, the ASPD group exhibited more blunted response to fenfluramine challenge compared to the no-ASPD group especially in the later part of the experiment. For instance, delta prolactin (e.g. change from baseline) was significantly lower for the ASPD group at 240min whereas drug levels were no different for the two groups. Correlation analyses showed significant inverse correlations between prolactin area-under-the curve (AUC) and Child Behavioral Check

List (CBCL) scores on aggression (r =-.45, p =.011), delinquency (r =-.41, p =.028) and externalizing problems (r =-.45; p =.015).
Conclusions: The participants in this sample were prospectively studied at two different time points and the relation between childhood prolactin response-a proxi measure for serotonin function-and the development of ASPD was confirmed independently for these two follow-ups. Individuals with ASPD showed significantly lower serotonergic response in comparison to participants without ASPD. These findings further suggest that youth with ADHD who also exhibit low serotonergic activity might be at elevated risk for the development of ASPD

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Neuropsychopharmacology. 2016;41:S540.

LISDEXAMFETAMINE DIMESYLATE (LD) COMBINED WITH REGULAR RELEASE STIMULANTS IN ADULT ATTENTION DEFICIT HYPERACTIVITY DISORDER (ADHD).

Abuzzahab F, Abuzzahab K, Kamsheh F.

Background: Our group had previously presented a poster on LD in ADHD at the 4th World Congress on ADHD in Milan, Italy on June 8th, 2013. The same poster was presented at the Neuroscience Education Institute's Psychopharmacology Congress in Colorado Springs, CO, and was later published. LD is a unique prodrug long-acting stimulant combining lysine with dextroamphetamine. After oral administration, LD is rapidly absorbed from the gastrointestinal tract and converted by hydrolytic activity of red blood cells to dextroamphetamine, which is responsible for its activity. The chemical designation for lisdexamfetamine dimesylate is (2 S)-2,6-diamino-N[(1-S)-methyl-2-phenylethyl] hexanamide dimethanesulfonate (See figure 2). LD was initially approved in the USA for children 6-12 years of age at doses of 30 mg, 50 mg, and 70 mg a day, and later for adults at the same doses1. Our previous poster was on adults with ADHD needing higher doses of LD than recommended up to 280 mg/day. One of the dilemmas of clinical pharmacology is that individuals who participate in research studies in pre-marketing are markedly different from those seen in clinics.
Methods: Outpatient charts of 50 adult patients, 29 males and 21 females, diagnosed with ADHD, were reviewed. They ranged in age between 18 and 71 with an average of 43 years ± 12.92 and an average body mass index of 28 kg/m2 ± 4.97. The 50 adult patients were split into two groups; one group with patients taking additional regular release central nervous system stimulants, and the other with patients who were not taking additional central nervous system stimulants.
Results: 35 out of 50 patients (equivalent to 70%) required additional regular release central nervous system stimulants, presumably because LD at the FDA approved dose of 70 mg/day failed to fully control their ADHD symptoms (See Figure 1). There were no statistical differences in age or body mass index between the 35 people who required additional medications and the 15 people who did not require additional medications. This group of 15 adults with ADHD who did not require additional central nervous system stimulants was too small for statistical purposes to achieve meaningful results.
Conclusions: In this preliminary report, charts of fifty adults with ADHD receiving LD at 70 mg/day were reviewed, and revealed that 70% required additional central nervous system stimulants. Outpatient charts indicate that the use of LD in doses higher than the maximum recommended ones in its package insert may or may not suggest that it is due to differences between the pre-marketing study populations and the ones seen in clinics. Sponsored in part by Psychopharmacology Fund and University of Minnesota Medical Foundation, Minneapolis, MN. Submitted to the American College of Neuropsychopharmacology in Hollywood, FL, December 2016

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Neuropsychopharmacology. 2016;41:S53.

CANNABIS USE IS ASSOCIATED WITH FRONTOPARIETAL STRUCTURAL AND FUNCTIONAL ABNORMALITIES AND EXECUTIVE DYSFUNCTION IN YOUNG ADULTS WITH AND WITHOUT ADHD.

Lisdahl K.

Background: Cannabis (CAN) use is on the rise in youth in the United States, with 23% of high school seniors and approximately 20% of college students reporting past month use (Johnston et al, 2015). This adolescent onset of CAN use coincides with significant neuromaturation, especially in frontoparietal regions (Giedd et al, 1006 Lenroot &Giedd, 2006; Sowell et al, 2002). Given this, the neurotoxic effects of substance use may be more pronounced in adolescents and emerging adults (Lisdahl et al, 2015). This talk will present findings from a series of studies examining the neurocognitive effects of CAN in adolescents and emerging adults.

Methods: Neuroimaging, neuropsychological, and substance use data was collected from regular CAN users and nonusing controls (CNT) across three independent NIDAfunded studies (range of abstinence 2-21 days; age range 16-25). For the first two studies (N =68; N =83), participants were recruited from the community and had to be either a CAN user (450 uses) or CNT (<5 lifetime uses) with minimal other illicit drug use (<20 occasions). Other exclusionary criteria included independent Axis I psychiatric disorder, major medical or neurologic disorder, premature birth or prenatal drug exposure, left-handedness, loss of consciousness 42 minutes. For the final study, CAN-using and CNT participants (N =120) were selected from a national longitudinal multi-site study (MTA) examining the trajectory of Attention Deficit Hyperactivity Disorder (ADHD). 120 participants were recruited for a neuroimaging, neuropsychology, and substance use study session. Exclusion criteria included other illicit drug use, excessive binge drinking, left-handedness, major medical or neurologic disorder.

Results: In the first set of studies, we demonstrate abnormal prefrontal and parietal volumes, prefrontal gyrification, and reduced executive functioning in regular CAN using young adults (Price et al, 2015; Shollenbarger et al, 2015; Lisdahl et al, 2012). In a follow-up study in adolescents and young adults after three weeks of monitored abstinence, we again found reduced selective attention and inhibitory control deficits (p'so.05), along with reduced left inferior frontal gyrus (IFG) (p =.005), left rostral anterior cingulate (ACC) (p =.009), right frontal pole (p =.03), and left frontal pole (p =.003) volumes (Lisdahl et al, under review). Finally, compared to CNTs, CAN users had abnormal cognitive control of affective stimuli connectivity, including blunted rIFG connectivity with medial prefrontal cortex (PFC), posterior cingulate, and increased connectivity with ACC, insula, precuneus, and parahippocampal regions (Lisdahl et al, under review). In a multi-site neuroimaging study (MTA) that prospectively followed children with and without ADHD into young adulthood, we found that CAN users demonstrated decreased cortical thickness in right superior frontal sulcus, ACC, and isthmus of cingulate gyrus regions and left superior frontal sulcus and precentral gyrus regions (Lisdahl et al., 2016).

Conclusions: Across three independent samples, young regular CAN users demonstrate abnormalities in frontoparietal structure. Further, we recently found abnormal functional brain response while engaging cognitive control of affective stimuli in frontolimbic and parietal regions. Potential limitations, future directions, and clinical implications will be discussed

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Neuropsychopharmacology. 2016;41:S134.

CHILDREN WITH ADHD AND SYMPTOMS OF OPPOSITE DEFIANT DISORDER IMPROVED IN BEHAVIOR WHEN TREATED WITH METHYLPHENIDATE AND ADJUVANT RISPERIDONE, THOUGH WEIGHT GAIN WAS ALSO OBSERVED.

Holsboer-Trachsler E, Jahangard L, Akbarian S, et al.

Background: Children with ADHD often also show symptoms of oppositional defiant disorders (ODD). We investigated the impact of adjuvant risperidone (RISP) to a standard treatment with methylphenidate (MPH) in children with ADHD and symptoms of ODD.

Methods: Inclusion criteria were as follows: 1. Diagnosis of ADHD (DSM-IV: 314) and ODD (DSM-IV 313.81); 2. Within the first 4 weeks: initial treatment of 1mg MPH/kg/d with no/very small symptoms improvements; 3. initial family counseling and psychoeducation with no improvements in behavior. Of the 172 children approached, 84 children met the inclusion criteria mean age: M = 8.55; 73.8% males) and took part in a double-blind, randomized, placebo-controlled, clinical trial lasting eight weeks. Participants were randomly

assigned either to the MPH+RISP (1.1mg/kg/d + 1mg/d) or to the MPH+PLCO (placebo) (1.1mg/kg/d) condition. Symptoms of ADHD and ODD, weight, height, and blood pressure were assessed at baseline, and at weeks 2, 4, 6 and 8.
Results: Symptoms of ADHD and ODD decreased over time, though the significant Time by Group interaction showed that symptoms improved more in the MPH+RISP than in the MPH only condition. In the MPH+RISP condition weight and waist circumference also increased over time.
Conclusions: Data suggest that adjuvant RISP improved symptoms in children with ADHD and co-occurring ODD, but weight gain and higher prolactine levels were also observed. This may become an issue, once children become adolescents, a period of life in which body shape and body self-image are closely linked to self-confidence and peer acceptance. The ethical committee of the Hamadan University of Medical Sciences (Hamadan, Iran) has approved the study, which was conducted in accordance with the ethical standards laid down in the Declaration of Helsinki. All participants and their parents signed the written informed consent

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Neuropsychopharmacology. 2016;41:S146-S147.

CORTICAL MATURATION DELAYS CHARACTERIZE ADHD IN A LARGE-SCALE MEGA-ANALYSIS ACROSS THE LIFE-SPAN PERFORMED BY THE ENIGMA-ADHD WORKING GROUP.

Hoogman M, Bralten J, Onnink M, et al.

Background: Neuroimaging studies show structural alterations of various brain regions in children and adults with ADHD. However, these studies are often underpowered and heterogeneous in their methods. After studying subcortical structures (Hoogman et al, 2015, Biological Psychiatry. 77:105S), the ENIGMA-ADHD Working Group now aims to study cortical measures across the life-span in the largest cross-sectional sample of participants with ADHD and controls to date.
Methods: A total of 34 sites from around the world are part of the ENIGMA-ADHD Working Group, a preliminary analysis was performed in data from 32 sites that had run the fully automated and validated segmentation software (FreeSurfer) to segment cortical thickness and cortical surface area of the areas listed in the Desikan-Killiany atlas. Case-control mega-analysis was carried out on all brain regions, taking age, gender, and site as covariates in the model. We also ran the same model adding Mean Thickness (in the thickness analyses) and Mean Surface area (in the surface area analyses) as a covariate. To understand the effects of age on cortical measures, stratified mega-analyses were carried out for children (ageo15years) and adults (age421years). Pvalues corrected for multiple comparisons using the Benjamini-Hochberg procedure (false discovery rate of 5%) are reported.
Results: In the combined analysis of all subjects, the results of 2055 participants with ADHD and 1821 controls showed significantly reduced thickness values in the temporal pole (Cohen's d:-0.16, pFDR = 4.28x10-5), fusiform gyrus (Cohen's d:-0.14, pFDR = 0.0003), precentral gyrus (Cohen's d:-0.12, pFDR = 0.002), entorhinal cortex (Cohen's d:-0.11, pFDR = 0.008), parahippocampal gyrus (Cohen's d:-0.09, pFDR = 0.04), and paracentral lobule (Cohen's d:-0.09, pFDR = 0.04). The stratified analysis in children (n ADHD = 1084, n controls = 1070) implicated the same regions as the combined analysis, only with larger effect sizes (e.g. temporal pole Cohen's d =-0.20 and fusiform gyrus Cohen's d =-0.21). Additional structures differing between childhood cases and controls were the lateral occipital cortex and the insula (Cohen's d-0.13 and-0.12, respectively). The stratified analysis in adults (nADHD = 549, ncontrols = 415) did not reveal any regions in the cortex showing significant differences between cases and controls. However, borderline significant effects were found in the lateral occipital cortex and the superior parietal cortex, with these regions appearing thicker in patients; Cohen's d: +0.19, pFDR = 0.08, and Cohen's d: +0.19, pFDR = 0.08, respectively. Including 'mean thickness' in the model did not change the results. The analysis for surface area revealed a strong global casecontrol effect of mean surface area, Cohen's d =-0.21, pFDR = 4.67x10-9, with no additional regional effects. When we performed the analysis in children only, the effect became stronger, Cohen's d =-0.29, pFDR =2.00x10-9. In contrast, in adults, no effect of case-control status was found on mean surface area.
Conclusions: We found six areas in the cortex to be thinner in cases compared with controls. These areas are mainly located in the temporal and frontal lobes. The strongest effects were present in the temporal pole and the fusiform gyrus. Both of these structures have strong connections with the amygdala, which matches with results of our first study, in which the largest effect size was for a volume decrease in the amygdala of

patients with ADHD, highlighting the importance of emotional processing in ADHD (Hoogman et al, 2015, Biological Psychiatry. 77:105S). Our results are also in line with previous work, showing links with impulsivity symptoms (McLaughlin et al, 2014, Biol Psychiatry. 76:629-638) and faster thinning in ADHD children in a longitudinal study for the fusiform gyrus (Shaw et al, 2011, Am J Psychiatry. 168:143-151), as well as increased activity (Wilbertz et al, 2015, World J Biol Psychiatry.Epub) and thinning in children with ADHD (Fern+índez-Jan et al, 2014, Psychiatry Res. 224:8-13) for the temporal pole. The apparent normalization observed in adults in this crosssectional study provides additional evidence for cortical maturational delays in ADHD patients earlier described in an earlier longitudinal study (Shaw et al, Proc Natl Acad Sci USA. 104:19649-19654)

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Neuropsychopharmacology. 2016;41:S337-S338.

COMMON GENETIC VARIATION IN OXYTOCIN RECEPTORS IS DIFFERENTIALLY ASSOCIATED WITH SOCIAL ABILITIES ACROSS NEURODEVELOPMENTAL DISORDERS.

Baribeau D, Dupuis A, Paton TA, et al.

Background: Children with autism spectrum disorder (ASD) or attention deficit hyperactivity disorder (ADHD) share many overlapping symptoms, including difficulties with social information processing. A large body of human and animal research has demonstrated associations between social abilities/behaviors and the oxytocin and/or vasopressin neuropeptide systems. Common genetic variation in the oxytocin or vasopressin receptors (OXTR and AVPR1a) may contribute to differences in social abilities in typically developing humans. The degree to which genetic differences in these receptors modify the severity of social impairments in children with neurodevelopmental disorders, such as ASD or ADHD, is less well studied. Whether the magnitude or direction of the effects of genetic differences in neuropeptide receptors on social abilities varies depending on the diagnosis of the individual is also unknown.

Methods: In this study, social abilities were assessed in a cohort of children with either autism spectrum disorder (ASD, n = 339) or attention deficit hyperactivity disorder (ADHD, n = 275) using the Reading the Mind in the Eyes Test (RMET) and the Social Communication Questionnaire (SCQ). Genotype was determined for four OXTR single nucleotide polymorphisms (SNPs) (i.e. rs53576, rs237887, rs13316193 and rs2254298), and AVPR1a RS3 microsatellite length, from blood/saliva samples. Social abilities were compared by genotype within and across diagnostic groups using regression models while accounting for ethnic differences.

Results: Several significant associations between neuropeptide receptor genotype and social abilities were detected; findings survived correction for multiple comparisons for OXTR rs237887, rs2254298 and rs53576. For these SNPs, interactions between genotype and diagnosis were highly significant. For OXTR rs53576 and rs2254298, the opposite direction of an association between genotype and social abilities was observed in the ASD group as compared to ADHD group; specifically, the risk-conferring variant in ASD was advantageous to social abilities in ADHD.

Conclusions: Results suggest that neuropeptide receptor gene polymorphisms may modulate the severity of social deficits in ASD and ADHD. However, specific common variants may not be inherently risk-conferring with respect to their impact on social abilities. Whether a genotype is advantageous or not may vary depending on the diagnostic context. Our findings therefore contribute to the often-conflicting literature regarding these SNPs and behavioral-genetic studies more generally, implicating potential diagnostic differences as one explanation for heterogeneity in findings

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Neuropsychopharmacology. 2016;41:S537.

NEURAL CORRELATES OF EMPIRICALLY DERIVED PATTERNS OF PSYCHIATRIC SYMPTOMS IN YOUTH.

Brotman M, Stoddard J, Kircanski K, et al.

Background: By conceptualizing domains of behavior transdiagnostically, the National Institute of Mental Health Research Domain Criteria (NIMH RDoC) initiative encourages studies examining the neural circuitry of dimensional traits that transcend traditional diagnostic boundaries. Among youth, symptoms of irritability,

anxiety, depression, and inattention/hyperactivity all are prominent dimensions of psychopathology. However, there is considerable cooccurrence among these different types of symptoms, possibly reflecting shared neurobiological vulnerabilities. Aggregating these symptom dimensions into naturallyoccurring clusters or 'symptom profiles' may account for such co-occurrence and provide empirically-derived alternatives to established DSM diagnoses. Such an approach may reveal neural signatures associated with specific combinations of symptoms. Here, we assess the neural correlates of multidimensional symptom classes derived through latent profile analysis (LPA). We hypothesize that different symptom profiles will be associated with distinct patterns of neural responses to stimuli depicting face emotions.

Methods: Two hundred youth aged 7 to 18 years with fMRI data were included in the LPA analysis. Parents and/or youth completed symptom measures assessing: depression, anxiety, irritability, and attention deficit hyperactivity disorder (ADHD). The fMRI task involved making implicit (i.e., gender) ratings of happy, angry, neutral, and fearful faces across a range of intensities. Several classes of symptoms emerged, hereafter referred to as LPA groups: (1) low levels of all symptoms (LOW); (2) high levels of all symptoms (HIGH); (3) high levels of irritability and ADHD, with moderate-to-high anxiety and depression (ANX/DEP+ IRR/ADHD); (4) moderate-to-high anxiety and depression (ANX/DEP-IRR/ADHD). fMRI analyses were conducted using AFNI. First, we modeled an omnibus three-way interaction to predict activation: LPA group x Face emotion x Emotion intensity. Follow-up analyses focused on the interactions of LPA group x Face emotion and LPA group x Emotion intensity. Analyses were thresholded voxelwise $p<0.005$, $K = 83$.

Results: Accuracy and reaction time did not differ across LPA groups. Neither the three-way interaction nor the LPA group x Emotion intensity analysis yielded significant findings. Two regions emerged as significant in the LPA group x Face emotion activation analyses: right dorsolateral prefrontal cortex (dlPFC) ($k = 104$, Peak xyz = 46.2, 18.8, 31.2; $F(6, 389.8) = 5.17$, $p<0.001$) and right fusiform gyrus ($k = 96$, Peak xyz = 41.2, 56.2,-16.2; $F(5.9, 383.4) = 5.11$, $p<0.001$). In the right dlPFC, the ANX/DEP-IRR/ADHD group exhibited hyperactivation in response fearful faces, relative to both the LOW group and ANX/DEP+ IRR/ADHD group (both pso0.05). In contrast, the ANX/DEP+ IRR/ADHD group exhibited hypoactivation to fearful faces relative to the LOW symptom group ($p<0.05$). Thus, ANX/DEP-IRR/ADHD youth and ANX/DEP+ IRR/ADHD youth exhibited opposing patterns of dlPFC activation to fearful faces. The level of dlPFC activation to fearful faces in the HIGH group was in between those of the other groups, and did not differ significantly from either of them. In the right fusiform gyrus, the HIGH group exhibited hypoactivation to fearful faces relative to both the LOW group and ANX/DEP-IRR/ADHD group (both pso0.05). The level of fusiform gyrus activation in the ANX/DEP+ IRR/ADHD group was similar to that in the HIGH group, but did not differ significantly from the other groups.

Conclusions: In studies applying the RDoC framework to fMRI data, researchers typically examine associations between individual symptom dimensions and brain activity, and sometimes examine interactions between symptom dimensions. However, these studies are limited due to comorbidity, and hence collinearity, among symptom domains. In this study, we leveraged a large, well-phenotyped sample to integrate multiple symptom dimensions into classes, and then examined associations between these classes and brain activity during an implicit face emotion processing task. The LPA groups exhibited differing patterns of activation to fearful faces in two regions: the dlPFC and the fusiform gyrus. The dlPFC mediates cognition, response inhibition, and motor control, and has been implicated in the pathophysiology of mood and anxiety disorders. Whereas ANX/DEP-IRR/ADHD showed hyperactivation to fearful faces, ANX/DEP+ IRR/ADHD showed hypoactivation to fearful faces in the dlPFC. These results suggest that there are unique pathophysiological correlates of anxiety and depressive symptoms based on whether they are comorbid with irritability and ADHD. This pathophysiological distinction may have treatment implications. Similarly, activation in the fusiform gyrus differentiated groups. Here, youth with high levels of all symptoms showed hypoactivation to fearful faces, and were most similar ANX/DEP+ IRR/ADHD. This finding suggests that the presence of high irritability and ADHD symptoms in youth is associated with unique pathophysiological markers. Additional work is needed to explore the stability and longitudinal clinical trajectories of these symptom classes, as well as corresponding neural correlates

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Neuropsychopharmacology. 2016;41:S473-S474.

ARE BRAIN-BEHAVIOR RELATIONSHIPS FOR INTERNALIZING AND EXTERNALIZING BEHAVIORS SIMILAR ACROSS CHILDREN WITH ASD, ADHD AND OCD?

Ameis S, Anagnostou E, Lerch J, et al.

Background: Externalizing (e.g. aggressive, noncompliant, oppositional) and internalizing (e.g., withdrawn, anxious, inhibited, depressed) behaviors are common among children with autism spectrum disorder (ASD), attention-deficit/hyperactivity disorder (ADHD), and obsessive-compulsive disorder (OCD). Our recent study indicated that structural connectivity within an orbitofrontal-amygdalar network was associated with externalizing behaviors in healthy children. (Ameis, et. al, Biological Psychiatry, 2014). Here, we explored whether relationships between externalizing and internalizing behaviours and orbitofrontal-amygdalar circuitry may be present in children with either ASD, ADHD or OCD.

Methods: Structural imaging and behavioral measures were acquired in 125 children recruited through the Province of Ontario Neurodevelopmental Disorders Network (ADHD: n = 41, Mean age = 9.4 ± 2, 7 females; OCD: n = 22, Mean age = 11.2 ± 2.4; ASD: n = 62, Mean age = 10.8 ± 3.2; 12 females). Cortical thickness measures across the cortex were derived from quality-controlled native MR images processed through the CIVET 1.1.12 pipeline. Average cortical thickness measures for each ROI within the AAL atlas were extracted. Regional volumes for amygdala were obtained using a validated, fully automatic label-fusion based segmentation method applied to MR images. Relationships between externalizing behaviors and internalizing (measured with the Child Behavior Checklist) and orbitofrontal cortex (OFC) thickness, amygdala volume, and orbito-amygdalar structural networks were examined using first-order linear fixedeffects models, after controlling for age, sex and total brain volume across children and adolescents with ASD, ADHD and OCD.

Results: Although no between-group differences in internalizing behaviors were found (OCD = 65 ± 9.2, ASD = 62.3 ± 10.9, ADHD = 61.7 ± 9.8, F2,125 =.8, p = 0.44), externalizing behaviors differed between groups (OCD = 55 ± 10.3, ASD = 58 ± 10.6, ADHD = 62 ± 8.9, F2,125 = 4.6, p =.01), with significant differences found between OCD and ADHD participants. While no relationship between orbitoamygdalar coupling and either externalizing or internalizing behaviours was found across children with ADHD, ASD and OCD, a strong relationship between orbito-amygdalar coupling and externalizing behaviours was present in OCD children only in the right OFC (F1,16 = 8.8, p = 0.009). A trend relationship was also shown between right OFC thickness and internalizing behaviors (F1,121 = 2.7, p = 0.1) across children with ASD, ADHD, and OCD. Finally, an inverse relationship between OFC thickness and externalizing behavior in OCD children only was found (left: F1,16 = 8,1, p = 0.01, right: F1,16 = 6.5, p = 0.02). No significant associations between externalizing or internalizing behaviors and amygdala volume were found.

Conclusions: No cross-cutting relationship between orbitoamygdalar circuit structure and externalizing behaviors was found across children with ASD, ADHD and OCD. However, orbito-amygdalar covariance was related to externalizing behaviors in children with OCD only, as was OFC thickness. These relationships are very similar to those we have previously found in healthy controls children. The greater variability (clinical heterogeneity) in externalizing scores in children with ADHD and ASD, compared to OCD, suggest that efforts to improve clinical subtyping may be necessary for detection of biomarkers of externalizing behavior that cut across these disorders. Finally, the potential association of OFC thickness with internalizing behaviour across disorders deserves further investigation as data collection continues in our sample

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Neuropsychopharmacology. 2016;41:S486-S487.

ADULT ADHD WITH ANXIETY DISORDER AND DEPRESSION COMORBIDITY IN A CLINICAL TRIAL COHORT.

Van Ameringen M, Patterson B, Simpson W, et al.

Background: Adult ADHD is highly comorbid with mood and anxiety disorders, with 85% of patients having at least one psychiatric comorbidity, and 60% having at least two. Results from the National Comorbidity Survey-Replication study revealed that when ADHD was used as the index disorder, social anxiety disorder (29.3%), specific phobia (22.7%), and PTSD (11.9%) were the three most common DSM-IV anxiety disorders. Relatively high levels of comorbidity were also observed with mood disorders and ADHD (38.3%). Although it has been hypothesized that anxiety may be a feature that is closely tied to the pathogenesis of the ADHD, it has also been proposed that ADHD with comorbid anxiety may represent a subtype of ADHD

or that patients with ADHD and comorbid anxiety are phenotypically different from those with the pure disorder. The presence of anxiety comorbidity in adult ADHD has been associated with additive clinical effects, leading to more global impairment, poorer outcome, greater resistance to treatment and increased costs of illness. ADHD with comorbid anxiety disorders has also been associated with greater degrees of inattention. Stimulant medications are the first-line agents in the treatment of childhood ADHD and have demonstrated efficacy in adult ADHD. Few studies have examined the efficacy of ADHD treatments within these comorbid populations, as the bulk of the pharmacotherapy literature has examined the pure disorder. Only two randomized controlled trials have specifically examined adult ADHD with comorbidity. Adler and colleagues (2009) examined the use of atomoxetine in adult patients with ADHD and comorbid social anxiety disorder and found that patients treated with atomoxetine had significantly higher reductions in both ADHD ($p<0.001$) and social anxiety symptoms ($p<0.001$), when compared to placebo. RÂsler et al., 2010 examined the effects of extended release methylphenidate (MPH) on emotional symptoms of ADHD in a 24-week study. Extended-release MPH demonstrated improvements in emotional lability and dysregulation as well as improvements in obsessive compulsive disorder symptoms, as measured by a sub-scale. No change in anxiety, phobia or major depression symptoms were found. There have also been two studies using MPH compounds which have allowed mild comorbid depression or anxiety conditions. In one study, 9% of participants had a current comorbid condition and in the other, 80% had a lifetime mood disorder and 28% had a lifetime anxiety disorder. Both studies found that treatment response to MPH was not moderated by current or lifetime history of mood or anxiety disorders. Lisdexamfetamine dimesylate (LDX) is a central nervous system (CNS) stimulant with a unique chemical structure, and has been found to be efficacious in both child, adolescent and adult ADHD. Given the high degree of comorbidity between anxiety disorders and ADHD, and the limited evidence to guide clinicians on treatment, we are conducting a prospective trial examining adult ADHD with comorbidity. As this study is ongoing, this poster will present a preliminary analysis of the impact of anxiety and mood comorbidity on Adult ADHD symptom severity and functional impairment.

Methods: In this study, we examined the relationship between ADHD, anxiety and mood symptom severity using the clinician-rated ADHD-Rating Scale (ADHD-RS), the Barkley Adult ADHD Rating Scale (BAARS-IV), with the Overall Anxiety Severity and Impairment Scale (OASIS), the Revised Padua Inventory, the Panic and Agoraphobia Scale (PAS), the GAD-7, the Social Phobia Inventory (SPIN), the Quick Inventory of Depressive Symptoms (QID-SR-16), and the the Clinical Global Impression-Severity Scale (CGI-S). In addition, we examined the relationship between ADHD symptom severity, anxiety and mood comorbidity and functional impairment using the Sheehan Disability Scale (SDS) and the Weiss Functional Impairment Rating Scale (WFIRS). The sample was comprised of adult ADHD participants entering a randomized, double-blind, 18-week cross-over trial of flexibly-dosed LDX in the treatment of Adults (aged 18-65) with ADHD and anxiety disorder or depression comorbidity, which is currently being conducted.

Results: Forty adult ADHD subjects were evaluated. The sample was 48% male, with a mean age of 33.6 ± 11.4 years, and mean scores on the ADHD-RS = 44.9 ± 6.0, CGIS = 5.9 ± 0.6, BAARS = 48.8 ± 9.4 suggestive of severe ADHD. Generalized Anxiety Disorder was the most common comorbid condition (92.5%), followed by SAD (62.5%) and OCD (37.5%). No significant differences were found between males and females and no significant correlations were found with the ADHD-RS, in terms of symptom severity, comorbidity, ADHD sub-type or impairment. A positive correlation was found between inattentive symptoms (BAARS) and impairment: WFIRS $r = 0.35, p = 0.03$; SDS $r = 0.60, p<0.001$; while hyperactivity-impulsivity(BAARS) were positively correlated to ADHD severity: ADHD-RS $r = 0.59, p<0.001$, CGI-S $r = 0.57, p<0.001$

Conclusions: Similar to previous findings, comorbidity had little impact on ADHD severity. This finding is contrary to the anxiety and mood disorder literature where comorbidity tends to increase the severity of the index disorder and has a significant impact on functional impairment and treatment response. Unlike prior reports which have found that women with ADHD had higher anxiety severity and impairment than men, we did not find any differences found between genders. Inattention symptoms appear to have a stronger impact on impairment, while hyperactive-impulsive symptoms are stronger indicators of ADHD severity

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Obesity. 2017;25:178-84.

NEURODEVELOPMENTAL DISORDERS ARE HIGHLY OVER-REPRESENTED IN CHILDREN WITH OBESITY: A CROSS-SECTIONAL STUDY.

Wentz E, et al.

Objective: To investigate prevalence of neurodevelopmental disorders in children with obesity and to compare body mass index (BMI) and metabolic profile in the children.

Methods: Seventy-six children (37 girls, 39 boys) were consecutively recruited from a university outpatient clinic specialized in severe obesity. Neurodevelopmental disorders including attention-deficit/hyperactivity disorder (ADHD), autism spectrum disorder (ASD), and developmental coordination disorder (DCD) were assessed using interviews and questionnaires. Neurodevelopmental diagnoses were collected retrospectively in medical records.

Results: BMI ranged between 1.9 and 5.9 SDS and age between 5.1 and 16.5 years. In 13.2% and 18.4% ASD and ADHD was assigned, respectively. In addition, 25% screened positive for DCD, 31.6% had at least one neurodevelopmental disorder, and 18.4% had a parent who screened positive for adult ADHD. Girls with ASD/ADHD had higher BMI SDS than girls without neurodevelopmental disorder (P = 0.006).

Conclusions: One third of children with obesity referred to specialist centers have a neurodevelopmental disorder including deviant motor skills, and these problems may deteriorate weight status. One fifth of the parents exhibit ADHD symptomatology which could partly explain the poor adherence by some families in obesity units. Future obesity therapy could benefit from incorporating a neurodevelopmental treatment approach

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Pediatr Int. 2016.

NUTRITIONAL STATUS AND FEEDING PROBLEMS IN PEDIATRIC ATTENTION DEFICIT-HYPERACTIVITY DISORDER.

Sha'ari N, Manaf ZA, Ahmad M, et al.

Background: Children with attention deficit-hyperactivity disorder (ADHD) may be at risk of nutrient deficiency due to the inability to sit through meals. This comparative cross-sectional study was therefore carried out to determine the nutritional status and feeding problems of ADHD children aged 4-12 years.

Methods: Sociodemographic data, anthropometric measurements and 3 day dietary intake record were collected from 54 ADHD children and 54 typical development (TD) children. The Behavioral Pediatrics Feeding Assessment Scale was used to assess feeding problems.

Results: Mean subject age was 8.6 ± 2.1 years. On anthropometric assessment, 11.1% of the ADHD children had wasting, while 1.9% had severe wasting. In contrast, none of the TD children had wasting. Approximately 5.6% of the ADHD children had stunting, as compared with 3.7% of the TD children, while none of the TD children had severe stunting compared with 3.7% of the ADHD children. More than half of the ADHD children had mid-upper arm circumference (MUAC) below the 5th percentile, indicating undernutrition, compared with only 35.2% of TD children. More than one-third of the ADHD children had feeding problems compared with 9.3% of TD children. There was a significant negative relationship between the ADHD children's feeding problems and bodyweight (r = -0338, P = 0.012), body mass index (r = -0322, P = 0.017) and MUAC (r = -0384, P = 0.004).

Conclusion: Almost half of the ADHD children had suboptimal nutrition compared with 11.1% of the TD children. It is imperative to screen ADHD children for nutritional status and feeding problems to prevent negative health impacts later on

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Pharmacopsychiatry. 2015;25.

CHILDREN SUFFERING FROM ADHD IMPROVED IN BEHAVIOR WHEN TREATED WITH METHYLPHENIDATE AND ADJUVANT RISPERIDONE, COMPARED TO METHYLPHENIDATE ONLY, THOUGH WEIGHT GAIN WAS ALSO OBSERVED-RESULTS FROM A RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED CLINICAL TRIAL.

Sadeghi Bahmani D, Jahangard L, Akbarian S, et al.

Objectives: Whereas prevalence rates for attention-deficit/hyperactivity disorder (ADHD) have not increased over the last three decades, the need for further treatment options is still pertinent given the heavy burden this disorder places both on children who suffer from it and their primary caregivers (e.?g., parents, teachers, sports coaches). Psychopharmacological treatment has typically involved methylphenidate (MPH) in various dosages. In the search for further treatment options, we investigated the impact of adjuvant risperidone (RISP) on ADHD symptoms and weight.

Method: Eighty four children suffering from ADHD (mean age: M?=?8.55; 73.8% males) took part in a double-blind, randomized, placebo-controlled, clinical trial lasting eight weeks. Participants were drug-naïve. They were randomly assigned either to the MPH + RISP or to the MPH + PLCO (placebo) condition. ADHD symptoms, weight, height, and blood pressure were assessed at baseline, and at weeks 2, 4, 6 and 8.

Results: ADHD symptoms such as oppositional behavior, hyperactivity and anxiety decreased over time, though the significant Time by Group interaction showed that symptoms improved more in the MPH + RISP than in the MPH only condition. Compared to the MPH only condition, in the MPH + RISP condition weight and waist circumference also increased over time.

Conclusions: Data suggest that adjuvant RISP improves symptoms in children with ADHD. On the other hand, weight gain was also observed

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PLoS ONE. 2016;11.

USING FUNCTIONAL OR STRUCTURAL MAGNETIC RESONANCE IMAGES AND PERSONAL CHARACTERISTIC DATA TO IDENTIFY ADHD AND AUTISM.

Ghiassian S, Greiner R, Jin P, et al.

A clinical tool that can diagnose psychiatric illness using functional or structural magnetic resonance (MR) brain images has the potential to greatly assist physicians and improve treatment efficacy. Working toward the goal of automated diagnosis, we propose an approach for automated classification of ADHD and autism based on histogram of oriented gradients (HOG) features extracted from MR brain images, as well as personal characteristic data features. We describe a learning algorithm that can produce effective classifiers for ADHD and autism when run on two large public datasets. The algorithm is able to distinguish ADHD from control with hold-out accuracy of 69.6% (over baseline 55.0%) using personal characteristics and structural brain scan features when trained on the ADHD-200 dataset (769 participants in training set, 171 in test set). It is able to distinguish autism from control with hold-out accuracy of 65.0% (over baseline 51.6%) using functional images with personal characteristic data when trained on the Autism Brain Imaging Data Exchange (ABIDE) dataset (889 participants in training set, 222 in test set). These results outperform all previously presented methods on both datasets. To our knowledge, this is the first demonstration of a single automated learning process that can produce classifiers for distinguishing patients vs. controls from brain imaging data with above-chance accuracy on large datasets for two different psychiatric illnesses (ADHD and autism). Working toward clinical applications requires robustness against realworld conditions, including the substantial variability that often exists among data collected at different institutions. It is therefore important that our algorithm was successful with the large ADHD-200 and ABIDE datasets, which include data from hundreds of participants collected at multiple institutions. While the resulting classifiers are not yet clinically relevant, this work shows that there is a signal in the (f)MRI data that a learning algorithm is able to find. We anticipate this will lead to yet more accurate classifiers, over these and other psychiatric disorders, working toward the goal of a clinical tool for high accuracy differential diagnosis

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PLoS ONE. 2017;12.

ASSESSMENT OF ATTENTION DEFICITS IN ADOLESCENT OFFSPRING EXPOSED TO MATERNAL TYPE 1 DIABETES.

Bytoft B, Knorr S, Vlachova Z, et al.

Objective: The aim of this study was to examine the potential association between intrauterine exposure to maternal diabetes and attention deficits in the offspring.

Research design and methods: Adolescent offspring of a prospectively followed cohort of women with type 1 diabetes (n = 269) and a control group from the background population (n = 293) participated in a followup assessment in 2012-2013. We used scores from Conners Continuous Performance Test II to assess attention and based on a principal component analysis we evaluated scores on five different attention factors: focused attention, vigilance, hyperactivity/impulsivity, sustained attention and response style.

Results: A higher frequency of the exposed offspring had a parent/self-reported use of Attention Deficit Hyperactivity Disorder (ADHD) medication compared to the control group (2.2% vs. 0.0%, p = 0.01). Clinical significant differences between adolescents exposed to maternal diabetes and unexposed controls were not found in either single scores on Conners Continuous Performance Test or on any of the five attention factors identified.

Conclusions: Exposure to maternal type 1 diabetes did not seem to increase the risk of attention deficits in the adolescent offspring. However, a higher self-reported use of ADHD medication in the exposed group could suggest a difference in attention not revealed by the applied test

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Psychiatry Res Neuroimaging. 2017;261:20-28.

ANOMALOUS SUBCORTICAL MORPHOLOGY IN BOYS, BUT NOT GIRLS, WITH ADHD COMPARED TO TYPICALLY DEVELOPING CONTROLS AND CORRELATES WITH EMOTION DYSREGULATION.

Seymour KE, Tang X, Crocetti D, et al.

There has been limited investigation of volume and shape difference in subcortical structures in children with ADHD and a paucity of examination of the influence of sex on these findings. The objective of this study was to examine morphology (volume and shape) of subcortical structures and their association with emotion dysregulation (ED) in girls and boys with ADHD as compared to their typically-developing (TD) counterparts. Participants included 218 children ages 8ΓÇô12 years old with and without DSM-IV ADHD. Structural magnetic resonance images were obtained, and shape analyses were conducted using large deformation diffeomorphic metric mapping (LDDMM). Compared to TD boys, boys with ADHD showed reduced volumes in the bilateral globus pallidus and amygdala. There were no volumetric differences in any structure between ADHD and TD girls. Shape analysis revealed localized compressions within the globus pallidus, putamen and amygdala in ADHD boys relative to TD boys, as well as significant correlations between increased ED and unique subregion expansion in right globus pallidus, putamen, and right amygdala. Our findings suggest a sexually dimorphic pattern of differences in subcortical structures in children with ADHD compared to TD children, and a possible neurobiological mechanism by which boys with ADHD demonstrate increased difficulties with ED

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Psychol Assess. 2015 Sep;27:1037-52.

THE CHILD CONCENTRATION INVENTORY (CCI): INITIAL VALIDATION OF A CHILD SELF-REPORT MEASURE OF SLUGGISH COGNITIVE TEMPO.

Becker SP, Luebbe AM, Joyce AM.

Sluggish cognitive tempo (SCT) is characterized by excessive daydreaming, mental confusion, slowness, and low motivation. Several teacher- and parent-report measures of SCT have recently been developed but a child self-report measure of SCT does not yet exist despite clear links between SCT and internalizing psychopathology (for which self-report is often desired). This study examined the initial reliability and validity of the Child Concentration Inventory (CCI), a child self-report measure of SCT symptoms, in a school-based sample of 124 children (ages 8-13; 55% female). Children completed the CCI and measures of academic/social functioning, emotion regulation, and self-esteem. Teachers completed measures of

psychopathology symptoms (including SCT) and academic/social functioning. Although exploratory structural equation modeling (ESEM) supported a 3-factor model of the CCI (consisting of slow, sleepy, and daydreamer scales closely resembling the factor structure of the parent-report version of this measure), bifactor modeling and omega reliability indices indicated that the CCI is best conceptualized as unidimensional. CCI scores were significantly correlated with teacher-rated SCT and were statistically distinct from teacher-rated ADHD and child-rated anxiety/depression. After controlling for sex, grade, and other psychopathology symptoms, the CCI total score was significantly associated with poorer child-reported academic/social functioning and self-worth in addition to increased loneliness and emotion dysregulation. Child ratings on the CCI were moderately to strongly correlated with poorer teacher-rated academic/social functioning but these associations were reduced to nonsignificance after controlling for demographics and other psychopathology symptoms. Findings provide preliminary support for the CCI, and future directions include replication with adolescents and clinical samples in order to further examine the CCI's factor structure, reliability, validity, and clinical utility

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Psychol Med. 2016 Apr;46:1225-38.

DIFFERENT NEURAL SUBSTRATES FOR EXECUTIVE FUNCTIONS IN YOUTHS WITH ADHD: A DIFFUSION SPECTRUM IMAGING TRACTOGRAPHY STUDY.

Chiang HL, Chen YJ, Shang CY, et al.

BACKGROUND: The relationship between white-matter tracts and executive functions (EF) in attention deficit hyperactivity disorder (ADHD) has not been well studied and previous studies mainly focused on frontostriatal (FS) tracts. The authors explored the microstructural property of several fibre tracts hypothesized to be involved in EF, to correlate their microstructural property with EF, and to explore whether such associations differ between ADHD and typically developing (TD) youths.

METHOD: We assessed 45 youths with ADHD and 45 individually matched TD youths with a computerized test battery for multiple dimensions of EF. From magnetic resonance imaging, FS tract, superior longitudinal fasciculus (SLF), arcuate fasciculus (AF) and cingulum bundle (CB) were reconstructed by diffusion spectrum imaging tractography. The generalized fractional anisotropy (GFA) values of white-matter tracts were computed to present microstructural property of each tract.

RESULTS: We found lower GFA in the left FS tract, left SLF, left AF and right CB, and poorer performance in set-shifting, sustained attention, cognitive inhibition and visuospatial planning in ADHD than TD. The ADHD and TD groups demonstrated different association patterns between EF and fibre tract microstructural property. Most of the EF were associated with microstructural integrity of the FS tract and CB in TD youths, while with that of the FS tract, SLF and AF in youths with ADHD.

CONCLUSIONS: Our findings support that the SLF, AF and CB also involve in a wide range of EF and that the main fibre tracts involved in EF are different in youths with ADHD

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Psychol Med. 2016 Apr;46:1277-87.

SPECIFIC COGNITIVE-NEUROPHYSIOLOGICAL PROCESSES PREDICT IMPULSIVITY IN THE CHILDHOOD ATTENTION-DEFICIT/HYPERACTIVITY DISORDER COMBINED SUBTYPE.

Bluschke A, Roessner V, Beste C.

BACKGROUND: Attention-deficit/hyperactivity disorder (ADHD) is one of the most prevalent neuropsychiatric disorders in childhood. Besides inattention and hyperactivity, impulsivity is the third core symptom leading to diverse and serious problems. However, the neuronal mechanisms underlying impulsivity in ADHD are still not fully understood. This is all the more the case when patients with the ADHD combined subtype (ADHD-C) are considered who are characterized by both symptoms of inattention and hyperactivity/impulsivity.

METHOD: Combining high-density electroencephalography (EEG) recordings with source localization analyses, we examined what information processing stages are dysfunctional in ADHD-C (n = 20) compared with controls (n = 18).

RESULTS: Patients with ADHD-C made more impulsive errors in a Go/No-go task than healthy controls. Neurophysiologically, different subprocesses from perceptual gating to attentional selection, resource allocation and response selection processes are altered in this patient group. Perceptual gating, stimulus-driven attention selection and resource allocation processes were more pronounced in ADHD-C, are related to activation differences in parieto-occipital networks and suggest attentional filtering deficits. However, only response selection processes, associated with medial prefrontal networks, predicted impulsive errors in ADHD-C.
CONCLUSIONS: Although the clinical picture of ADHD-C is complex and a multitude of processing steps are altered, only a subset of processes seems to directly modulate impulsive behaviour. The present findings improve the understanding of mechanisms underlying impulsivity in patients with ADHD-C and might help to refine treatment algorithms focusing on impulsivity

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Psychol Med. 2016 May;46:1485-96.

DUAL NEUROCIRCUITRY DYSFUNCTIONS IN DISRUPTIVE BEHAVIOR DISORDERS: EMOTIONAL RESPONDING AND RESPONSE INHIBITION.

Hwang S, Nolan ZT, White SF, et al.

BACKGROUND: To determine the functional integrity of the neural systems involved in emotional responding/regulation and response control/inhibition in youth (age 10-18 years) with disruptive behavioral disorders (DBDs: conduct disorder and/or oppositional defiant disorder) as a function of callous-unemotional (CU) traits.
METHOD: Twenty-eight healthy youths and 35 youths with DBD [high CU (HCU), n = 18; low CU (LCU), n = 17] performed the fMRI Affective Stroop task. Participants viewed positive, neutral, and negative images under varying levels of cognitive load. A 3-way ANOVA (groupxemotion by task) was conducted on the BOLD response data.
RESULTS: Youth with DBD-HCU showed significantly less activation of ventromedial prefrontal cortex (vmPFC) and amygdala in response to negative stimuli, compared to healthy youth and youth with DBD-LCU. vmPFC responsiveness was inversely related to CU symptoms in DBD. Youth with DBD-LCU showed decreased functional connectivity between amygdala and regions including inferior frontal gyrus in response to emotional stimuli. Youth with DBD (LCU and HCU) additionally showed decreased insula responsiveness to high load (incongruent trials) compared to healthy youth. Insula responsiveness was inversely related to ADHD symptoms in DBD.
CONCLUSIONS: These data reveal two forms of pathophysiology in DBD. One associated with reduced amygdala and vmPFC responses to negative stimuli and related to increased CU traits. Another associated with reduced insula responses during high load task trials and related to ADHD symptoms. Appropriate treatment will need to be individualized according to the patient's specific pathophysiology

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Psychopharmacology. 2017;234:403-20.

REDUCED INATTENTION AND HYPERACTIVITY AND IMPROVED COGNITION AFTER MARINE OIL EXTRACT (PCSO-524-«) SUPPLEMENTATION IN CHILDREN AND ADOLESCENTS WITH CLINICAL AND SUBCLINICAL SYMPTOMS OF ATTENTION-DEFICIT HYPERACTIVITY DISORDER (ADHD): A RANDOMISED, DOUBLE-BLIND, PLACEBO-CONTROLLED TRIAL.

Kean JD, Sarris J, Scholey A, et al.

Introduction: This study investigated the effects of a marine oil extract (PCSO-524-«) on inattention, hyperactivity, mood and cognition in children and adolescents. PCSO-524-« is a standardised lipid extract of the New Zealand green-lipped mussel and is an inflammatory modulator that inhibits the 5±lipoxygenase and cyclooxygenase pathways and decreases concentrations of the pro-inflammatory arachidonic acid (AA).
Methods: PCSO-524-« or a matched placebo was administered for 14-áweeks to 144 participants (123 males/21 females; mean age 8.7-áyears) with high hyperactivity and inattention in a randomised, double-blind, placebo-controlled study. The primary outcome was the Conners Parent Rating Scale assessing parental reports of behavioural problems. Secondary outcomes assessed changes in cognition and mood.

Results: The results of the present study did not support the hypothesis that PCSO-524-« improves parental reports of hyperactivity, inattention and impulsivity in children ages 6 to 14-áyears over placebo. Repeated measures ANOVA on post hoc subsample analysis indicated significant improvements in hyperactivity (p-á=-á0.04), attention (p-á=-á0.02), learning (p-á=-á0.05) and probability of ADHD (p-á=-á0.04) with a medium to large average effect size (d-á=-á0.65) in those children who did not meet criteria for combined hyperactivity and inattention. Furthermore, significant improvements in the PCSO-524-« group were indicated in a whole sample repeated measures ANCOVA on recognition memory between baseline and week 8 over placebo (p-á=-á0.02, d-á=-á0.56); this difference was not sustained at week 14.
Conclusions: The results presented indicate that PCSO-524-« may be beneficial in reducing levels of hyperactivity and inattention in a population of children with clinical and subclinical symptoms of ADHD

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Res Dev Disabil. 2017;61:44-54.

MATHEMATICAL LEARNING DISABILITIES AND ATTENTION DEFICIT AND/OR HYPERACTIVITY DISORDER: A STUDY OF THE COGNITIVE PROCESSES INVOLVED IN ARITHMETIC PROBLEM SOLVING.

Iglesias-Sarmiento V, et al .

Background The purpose of this study was to examine the contribution of cognitive functioning to arithmetic problem solving and to explore the cognitive profiles of children with attention deficit and/or hyperactivity disorder (ADHD) and with mathematical learning disabilities (MLD).
Methods The sample was made up of a total of 90 students of 4th, 5th, and 6th grade organized in three: ADHD (n-á=-á30), MLD (n-á=-á30) and typically achieving control (TA; n-á=-á30) group. Assessment was conducted in two sessions in which the PASS processes and arithmetic problem solving were evaluated.
Results The ADHD group's performance in planning and attention was worse than that of the control group. Children with MLD obtained poorer results than the control group in planning and simultaneous and successive processing. Executive processes predicted arithmetic problem solving in the ADHD group whereas simultaneous processing was the unique predictor in the MLD sample.
Conclusions Children with ADHD and with MLD showed characteristic cognitive profiles. Groups problem-solving performance can be predicted from their cognitive functioning

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Sleep Science. 2016;9:158-63.

THE RELATIONSHIP BETWEEN EPILEPSY, SLEEP DISORDERS, AND ATTENTION DEFICIT HYPERACTIVITY DISORDER (ADHD) IN CHILDREN: A REVIEW OF THE LITERATURE.

Neto FK, Noschang R, Nunes ML.

Objective To analyze the relationship between epilepsy, sleep disorders, and attention deficit hyperactivity disorder (ADHD).
Bibliographic search A literature search of the PubMed database was performed using the following key words: epilepsy, sleep, and ADHD. In total, 91 articles were located in PubMed, 34 were selected for abstract reading and twelve articles were reviewed, in which the main objectives were examine the relationship between epilepsy, sleep and ADHD from several perspectives, including epidemiology, effect of comorbidities on academic performance and the factors leading to diagnostic difficulties among these three disorders
Results Among the main findings, there were difficulties to start and maintain sleep in patients with epilepsy and ADHD, reduction in sleep efficiency, decreased seizure threshold, as well as behavioral and cognitive deficits in both groups.
Conclusions It is important to know which symptom is the predominant one. For this reason, children and adolescents with epilepsy, ADHD and sleep disorders need to be assessed carefully before initiating treatment. Our review concluded that there is an important link in this pathological triad

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Stat Med. 2016 May;35:1595-615.

COMPARING DYNAMIC TREATMENT REGIMES USING REPEATED-MEASURES OUTCOMES: MODELING CONSIDERATIONS IN SMART STUDIES.

Lu X, Nahum-Shani I, Kasari C, et al.

A dynamic treatment regime (DTR) is a sequence of decision rules, each of which recommends a treatment based on a patient's past and current health status. Sequential, multiple assignment, randomized trials (SMARTs) are multi-stage trial designs that yield data specifically for building effective DTRs. Modeling the marginal mean trajectories of a repeated-measures outcome arising from a SMART presents challenges, because traditional longitudinal models used for randomized clinical trials do not take into account the unique design features of SMART. We discuss modeling considerations for various forms of SMART designs, emphasizing the importance of considering the timing of repeated measures in relation to the treatment stages in a SMART. For illustration, we use data from three SMART case studies with increasing level of complexity, in autism, child attention deficit hyperactivity disorder, and adult alcoholism. In all three SMARTs, we illustrate how to accommodate the design features along with the timing of the repeated measures when comparing DTRs based on mean trajectories of the repeated-measures outcome

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Ther Adv Psychopharmacol. 2016;6:384-85.

LOW-DOSE QUETIAPINE COMPLEMENTS STIMULANT RESPONSE IN ATTENTION DEFICIT HYPERACTIVITY DISORDER AND MORE.

Naguy A.

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Tijdschr Psychiatr. 2016;58:446-54.

PREVALENCE OF THE USE OF PSYCHOACTIVE MEDICATION TO TREAT YOUNG PERSONS WITH AUTISM SPECTRUM DISORDER IN THE PROVINCE OF ANTWERP, BELGIUM.

Heyde E, Dhar M, Hellemans H, et al.

BACKGROUND: Very little information is available concerning the prevalence of the use of medication for treatment of individuals with autism spectrum disorder (ASD), particularly in European countries. Earlier studies have shown that a large number of patients with ASD use at least one psychoactive drug and that the numbers are increasing. Even in the nineties, studies suggested that the frequent use of psychoactive medication was widespread, although at the time there were only limited grounds for this assumption. AIM: To assess the prevalence with which psychoactive medication and complementary and alternative medicine (CAM) are being used for treating young people with ASD, and also to investigate relations between medication use and a number of individual characteristics that are included in the Behavioral Model of Health Service Use.

METHOD: The study sample (0-17 years) in the province of Antwerp, Belgium, was recruited by various means. We used a questionnaire that had been previously used in North American studies and that had to be completed by the parents of the young persons involved in the study.

RESULTS: We included data from 263 questionnaires. In our sample 42.6% of the young persons used one or more one psychoactive drug. More than 12.2% used more than one drug. The most frequently used psychoactive drugs were ADHD-medication (31.6%) and antipsychotics (16.7%). About 14% used at least one CAM. We found a positive relationship between the use of medication and psychiatric comorbidity and/or epilepsy, the severity of autism and the parents' living conditions.

CONCLUSION: We found a relatively low use of antipsychotics, antidepressants, mood stabilisers and sedatives, the prevalence being lower that that reported in North American studies. Our findings appear to be in accordance with current clinical guidelines

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Trials. 2017;18.

NIRS-BASED NEUROFEEDBACK TRAINING IN A VIRTUAL REALITY CLASSROOM FOR CHILDREN WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER: STUDY PROTOCOL FOR A RANDOMIZED CONTROLLED TRIAL.

Blume F, Hudak J, Dresler T, et al.

Background: Children with attention-deficit/hyperactivity disorder (ADHD) suffer from attention deficits, motor hyperactivity, and impulsive behaviour. These impairments are experienced at home, at school, and with friends. Functional imaging studies show that ADHD behaviour and impairments in executive functions (EFs) are mirrored by aberrant neurophysiological functioning. Moreover, several studies show that ADHD behaviour, impairments in EFs, and a lack of self-control contribute to poor school performance. Non-pharmacological interventions such as neurofeedback training (NFT), for instance, aim at improving neurophysiological and neuropsychological functioning as well as behaviour. Consequently, NFT is expected to improve school performance, EFs, and self-control in children with ADHD. Generalization of acquired self-regulation skills from laboratory to real life is crucial for a transfer to everyday situations and is hypothesized to be facilitated via training using virtual reality (VR) environments. Consequently, experiencing NFT in VR is expected to yield greater effects than training in two dimensions (2D).
Methods/design: Ninety children with a clinical diagnosis of ADHD will be included in the study. Participants may be medicated or unmedicated. After random assignation to one of three conditions, all participants receive 15 training sessions of either near-infrared spectroscopy (NIRS)-based NFT in VR, NIRS-based NFT in 2D, or electromyogram-based biofeedback training in VR. ADHD symptoms, self-control, EF, health-related quality of life, school performance, and motor activity measured via parent, teacher, and child reports or objectively will be assessed before and after the intervention and at a 6 months follow-up. Furthermore, we are interested in parents' expectations about the training's effects.
Discussion: This is, to our knowledge, the first study investigating the efficacy of NFT for children with ADHD in a VR compared to a 2D environment. Furthermore, this study will contribute to the discussion about the efficacy and specific and unspecific effects of NFTs in children with ADHD. In addition to commonly assessed variables such as ADHD symptoms, NIRS and behavioural data obtained in EF measures, health-related quality of life, and parents' expectations about the intervention's effects, this study will investigate the effects on self-control, school performance, and motor activity.
Trial registration: ClinicalTrials.gov, NCT02572180. Registered on 19 November 2015

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Zhongguo Dang Dai Er Ke Za Zhi. 2016 Jul;18:594-98.

CORRELATION BETWEEN EVENT-RELATED POTENTIAL AND BEHAVIORAL PROBLEMS IN EARLY SCHOOL-AGE CHILDREN WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER .

Pu XJ, Dong X, Shen HJ, et al.

To investigate the cognitive characteristics in early school-age children with attention deficit hyperactivity disorder (ADHD) using event-related potential (ERP) and Achenbach Child Behavior Checklist (CBCL), as well as the correlation between ERP and behavioral problems. A total of 22 children aged 6-7 years with ADHD and 19 healthy children matched by age were enrolled. Continue Performance Test-AX (CPT-AX) was performed for ERP test. The amplitude and latency of N2 and P3 of Go and Nogo were compared. The CBCL was completed by the parents, and the correlation between behavioral factors and ERP was analyzed. The ADHD group had a significantly higher number of ERP omissions than the normal control group (10+/-8 vs 5+/-4; P<0.05), while the reaction time and number of commission errors showed no significant differences between the two groups (P>0.05). The ADHD group showed a significantly lower Go-N2 amplitude than the normal control group (-8+/-5 muV vs -10+/-4 muV; P<0.05). In the ADHD group, the detection rates of hyperactivity, attack, and discipline violation were 27%, 27% and 9% respectively. The scores on attack and discipline violation subscales were negatively correlated with the Go-N2 amplitude of ERP (r=-0.43 and -0.48 respectively; P<0.05), while the score on hyperactivity subscale was positively correlated with the latency of Go-P3 (r=0.50, P<0.05). The early school-age children with ADHD show the tendency to the impairment of

attention/executive function, but the inhibition function defect has not been noted. In early school-age children with ADHD, the behavioral problems such as hyperactivity, attack, and discipline violation are associated with ERP

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Zhongguo Dang Dai Er Ke Za Zhi. 2016 Jul;18:589-93.

CHARACTERISTICS OF ATTENTION IN SCHOOL-AGE CHILDREN WITH MILD AUTISM SPECTRUM DISORDER.

Wang J, Zhang J, Wang ZZ, et al.

To investigate the characteristics of attention in school-age children with mild autism spectrum disorder (ASD), and to provide a basis for clinical treatment. A total of 20 school-age children with mild ASD were enrolled, and the intermediate visual and auditory continuous performance test (IVA-CPT) was used to assess their attention. A total of 20 children with attention deficit hyperactivity disorder (ADHD) and 40 healthy children were enrolled as controls. Compared with the normal control group, the ASD group showed significantly lower scores of full scale attention quotient, full scale response control quotient, visual/auditory full scale response control quotient, visual/auditory prudence quotient, auditory perseverance quotient, visual consistency quotient, visual/auditory vigilance quotient, visual attention quotient, visual speed quotient, number of correct visual/auditory reactions, and visual mean reaction time of the second and third phases ($P<0.05$). Compared with the ADHD group, the ASD group showed significantly higher scores of full scale response control quotient and auditory consistency quotient ($P<0.05$), as well as significantly lower scores of visual vigilance quotient and visual speed quotient ($P<0.05$). School-age children with mild ASD have attention deficit mainly manifested as the defect in the ability to focus attention, which is similar to the defect in children with ADHD, but ASD children have a lower degree of attention control impairment compared with children with ADHD. The defect in the ability to focus visual attention is more severe than that in the ability to focus auditory attention, while there is no significant difference between the defects in visual and auditory attention control

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P.7.d.005 Do callous–unemotional traits modulate pharmacological treatment of aggression in children and adolescents with conduct disorder?

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Background: Children and adolescents with conduct disorder (CD) show repetitive and persistent patterns of aggressive behaviour and pose a significant public health problem and a worrisome social burden. The more severe forms of CD are often associated with callous-unemotional (CU) traits [1]. A growing literature suggests that several medications may be effective in the treatment of aggression, with varying degrees of efficacy, but the evidence to support use of diverse medications to treat aggression are limited and the effectiveness of medication treatments in real world clinical settings remains unclear.

Objectives: The purpose of this review was to systematically explore the evidence regarding medications for the treatment of aggression in children and adolescents with CD, investigating whether there is evidence to suggest which drugs are more effective relating to the presence of CU traits and the different subtypes of aggression.

Methods: We systematically searched for the most relevant published reviews and meta-analysis on the topic and individual trials published up to January 2016 that were not included in the previous reviews, using a range of research sources (PubMed, MEDLINE via Ovid SP, EMBASE via Ovid SP, PsycINFO via Ovid SP). Studies exploring the effect of medications on aggressive subjects (aged 5–18 years) with a diagnosis of CD were included. The primary outcome measure was the pre-post treatment change or means at end-point as assessed by ratings on validated scales for aggression, conduct problems and CU traits. Effect sizes were calculated when data were available.

Results: A total of 33 studies were included. Very few randomized double-blind trials have examined the efficacy of medication on aggression in children and adolescent with a primary diagnosis of CD, with only a few studies including more than 50% of subjects with CD within the total sample. This makes it difficult to generalize the findings into the overall CD population. Only three trials discriminated between different types of aggression, including CU traits.

Methylphenidate and risperidone showed the largest effects in the management of aggression in randomized controlled trials. Stimulant medications appear an important potential therapeutic option for aggression but this effect appears as a secondary outcome from clinical trials in the ADHD population with comorbid CD. Risperidone is the antipsychotic with the most evidence of efficacy on aggression, but the majority of double blind studies are performed on subjects with sub average IQ. Other antipsychotic agents appeared to show clinical efficacy on CD but the evidence is mainly restricted to that from open label trials. Low quality evidence supports a small effect of mood stabilizers and other agents.

Discussion: Effects on specific subtypes of aggression (i.e. instrumental aggression common in subject with limited prosocial emotions specifier or CU traits) are rarely investigated, making difficult to formulate recommendations for a tailored pharmacotherapy with regards the different forms of aggression. The complex and heterogeneous pathophysiology of the disorder suggests the need of proof-of-concept clinical studies to define effects of medication on specific neuropsychological domains.

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P.7.d.006 Methylphenidate effects on height and bone age in ADHD children. 24 month follow up within the prospective ADDUCE project

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Background: In Europe methylphenidate (MPH) is the first choice medication for ADHD). Positive effects on the core symptoms are supported by numerous trials, but stimulants may induce several common mild and transient as well as rare and severe adverse events, including growth reduction with the prolonged use [1]. Several studies have monitored changes in growth during medication, providing inconclusive results on growth suppression induced by medication; only very few studies investigated the rate of bone age as a sensible parameter to predict a possible impact on height. Growing more slowly but continuing to have a bone maturation at the normal rate can in fact reflect the possibility of not reaching its own growth potential [2].

Objectives: To evaluate, within the prospective, longitudinal, pharmacovigilance, EU funded project ADDUCE, whether methylphenidate for ADHD is associated with a statistically significant increase in long-term risk of negative effects on height and bone maturation and to explore the application of monitoring of bone age as a helpful tool for studying adverse developmental effects.

Methods: Height, Weight, BMI, Target Height, X-ray of left wrist and the prediction of adult height were collected from 44

drug naïve ADHD Italian children, aged 6–12, at three time points: baseline visit and after 12 and 24 months.

Results: According to the Italian growth norms the 44 ADHD included into the study presented with a normal growth pattern at the baseline visit: height Z-score was 0.06±1.13, weight Z-score 0.11±1.21, BMI Z-score 0.12±1.17 and the Target Height Z-score for the male population was 0.26±0.92. The bone age calculated by the Tanner and Whitehouse II method was 8.07±2.10, resulting slightly behind the chronological age of 8.75±1.72 although not in a clinically significant manner.

The 26 subjects retained into the study with a 24 month follow up presented with an adequate pattern of growth in terms of height (baseline Z score = 0.18±1.02 vs T24 Z score = 0.38±1.08) while BMI was slightly reduced after 24 months of treatment (baseline Z score = 0.14±1.16 vs T24 Z score = –0.04±1.22; p = 0.03). The bone age at the 24 month follow up time (10.97±2.18) was correctly aligned with the chronological age (10.85±1.69) evidencing a possible acceleration of bone maturation compared to the baseline measurements. The predicted adult height remained stable at each follow up time (baseline = 178.37±7.2; T12 = 177.18±7.8; T24 = 178.63±8.0).

Discussion: These results suggest that ADHD children present with a normal growth pattern in terms of height prior to starting medication and that this remains the case after 24 months of treatment. Medication may impact on weight during the first months of treatment with a significant reduction of BMI. The study of bone age indicated possible bone maturation acceleration, however the predicted adult height remained substantially stable at each follow up time indicating just a possible normalization of growth. Firm conclusions on the effects of medication on growth could be drawn only with a longer follow up at the reach of final height.

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P.7.d.007 Long-acting injectable atypical antipsychotics in adolescent population: an observational study

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Introduction: Second generation long-acting injectable antipsychotics (SG-LAIAs) are a valid strategy for the maintenance treatment of schizophrenia, recently approved by the European Medicines Agency in adult patients [1]. There is growing evidence that SG-LAIAs leads to a reduced risk of relapse compared with oral formulations [2]. However, except for a few case reports [3], safety and effectiveness of SG-LAIAs have not been studied in children and adolescent age groups. We set out to provide a clinical description of a sample of adolescent patients in whom off-label treatment with SG-LAIAs was commenced during inpatient admission.

Methods: All subjects admitted to our Children and Adolescent Inpatient Psychiatry Unit receiving off-label treatment with SG-LAIAs during 2015 were reviewed. A retrospective analysis of medical records was conducted, clinical diagnoses were established fulfilling DSM-5 criteria.

Results: Twelve out of a total of 55 patients with a psychotic disorder were identified (21.8%), plus 5 patients with other non-psychotic diagnoses. Two cases were excluded because SG-LAIA had been started prior to admission. Therefore, a total of 15 subjects (8 males) were included in the analysis. The mean age was 16.1 (SD = 1.6, range = 12–17) and 33.3% of patients were in foster care. Sixty percent presented truancy and drug use, mostly cannabis (53.3%). Although only 1 case was diagnosed with intellectual disability, borderline intelligence quotient was reported in 26.7% of cases.

Patients were admitted an average of 14.5 (SD = 8.1) days, with a mean score of 23 (SD = 8.6) in the Children's Global Assessment Scale (CGAS) at intake. Reasons for referral included disruptive behavior or aggression (93.3%), delusions (40%), negative symptoms (33.3%), hallucinations (26.6%) among others. Poor insight was reported in 80% of cases, in the rest of patients, awareness of disease were only partial. Main diagnoses at discharged included psychosis not otherwise specified (46.7%), disruptive behavior disorder (DBD) (33.3%), schizoaffective disorder (13.3%) and schizophrenia (6.7%); 46.6% presented comorbid attention-deficit/hyperactivity disorder. Many had a history of previous hospitalizations (93.3%) and oral antipsychotic treatment (100%). All patients had a history of poor treatment adherence (100%) and up to 46.7% had interrupted treatment altogether.

SG-LAIAs employed were aripiprazole (46.7%), risperidone (33.3%) and paliperidone palmitate (20%). Although they were generally well tolerated, 20% of patients presented mild short-term side-effects; 2 cases attributed to risperidone (rigidity and somnolence) and 1 to aripiprazole (akathisia). CGAS demonstrated clinical improvement at discharge (mean 58.3, SD = 8.1).

Discussion: Clinical experience from the current sample suggest that SG-LAIAs are an effective and safe – in the short term – treatment option during adolescence. Although most patients experienced psychotic disorders, a proportion of subjects received SG-LAIAs treatment due to DBD. Despite the fact that antipsychotic treatment is not approved for such indication, its off-label use in daily practice is well documented [4]. In our sample all patients were at special risk for treatment non-adherence, given the presence of factors such as drug use or poor insight, which may lead to increased risk of relapse [5]. Nevertheless, further research is needed so as to evaluate long-term safety and effectiveness of SG-LAIAs in this population.

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Importance of neuropsychiatric evaluation in children with primary monosymptomatic enuresis

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Keywords
Enuresis; Comorbidities; Tic disorder; Attention deficit hyperactivity disorder; Obsessive–compulsive disorder; Quality of life

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Summary

Background
Nocturnal enuresis (NE) is an involuntary voiding during sleep. It is a very common disorder in school-age children. Comorbid psychopathologies are common in patients affected by enuresis. According to the ICCS, the rate of behavioral and emotional disorders in children with enuresis is doubled compared with healthy control (HC) children.

Objective
The aim of the present study was to investigate the prevalence of neuropsychiatric comorbidities in children affected by NE.

Study design
Two hundred children with a diagnosis of enuresis were recruited from the Neuropsychiatric Unit of Catania University and 200 age-matched neurologically intact HC children were recruited from local schools. The inclusion criteria were a normal IQ and the absence of other pathological clinical conditions such as diabetes or kidney malformation. The exclusion criteria were failure to complete the initial evaluation or clinical/diagnostic procedures, inability (because of young age) to complete study questionnaires, and severe neurological or physical impairment.

Results
Age and gender proportions were not significantly different between the groups. In the NE group, 138 subjects (69%) had a familial history of NE, compared with 24 subjects (12%) in the HC group ($p < 0.01$). The NE group demonstrated significantly higher scores in the Child Behavior Check List, Conners' Multidimensional Anxiety Scale for Children, and the Child Depression Inventory compared than the HC group as well as the Yale Global Tic Severity Score and Child-Yale–Brown Obsessive Compulsive Scale scores ($p < 0.01$). Quality of life scores were significantly lower in the NE group than in the HCs group; specifically, between-group differences were significant in the relationship and self domains ($p > 0.01$ for both comparisons) (Figure).

Discussion
The present case-control study evaluates the prevalence of different neuropsychiatric comorbidities in children with NE as diagnosed according to the new ICCS criteria. An important finding was that neuropsychiatric conditions were more prevalent in NE patients than in age-matched HC subjects. To the best of our knowledge, this is the first study to report associations between enuresis and obsessive compulsive disorder as well as tic disorder, and is the first to describe the comparative psychopathological profiles of 200 children with enuresis and 200 matched HC children.

Conclusion
The results suggest that clinicians should not underestimate the effects of enuresis on psychosocial development. Childhood NE should be managed carefully and comprehensively in order to prevent the development of more serious behavioral problems in the future.

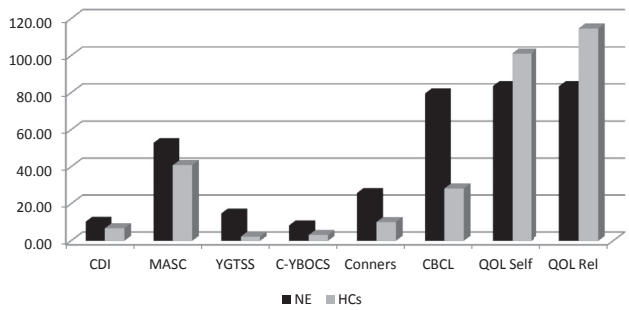

Figure Comparison between nocturnal enuresis patients and healthy control children ($p \leq 0.000$). CDI = Child Depression Inventory; MASC = Multidimensional Anxiety Scale for Children; YGTSS = Yale Global Tic Severity Score; C-YBOCS = Children-Yale–Brown Obsessive Compulsive Scale; CBCL = Child Behavior Check-List; QoL = Quality of life; Rel = relationship.

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Introduction

Nocturnal enuresis (NE) is an involuntary voiding that occurs in subjects who have not yet achieved bladder control. NE is a very common disorder in school-age children, occurring in 10% of 6-year-olds and in 5% of 10-year-olds [1]. Recently the Children's Continence Society (ICCS) [2] defined enuresis as intermittent (i.e., not continuous) wetting during sleep in children 5 years and older, where the term nocturnal can be added for clarity (i.e., enuresis and NE are synonyms).

Growing interest in the pathophysiology and etiology of enuresis has spurred the publication of more than 570 studies since 2009. This body of work uncovered subclinical behavioral symptoms such as sadness, embarrassment, and humiliation in children with enuresis that could not be technically classified as a disorder [3]. However, some studies suggest that comorbid psychopathologies are common in enuresis patients. In the general population, 10—15% of children have a behavioral disorder. According to the ICCS, the rate of behavioral disorders in children with enuresis is doubled [4]. Enuresis has been previously associated with attention deficit hyperactivity disorder (ADHD) [5,6], oppositional defiant disorder [7], and conduct disorders [8]. Moreover, patients and family members of patients with enuresis demonstrated lower quality of life global ratings in comparison with healthy control (HC) children [9,10], similar to observations in patients with chronic diseases such as epilepsy or asthma [11].

Therefore, we conducted the present exploratory case-control study to investigate the prevalence of neuropsychiatric comorbidities in children affected by NE.

Materials and methods

Study population

Subjects (patients and controls) were prospectively enrolled between October 2013 and September 2015. In total, 200 children with a diagnosis of primary monosymptomatic enuresis were recruited from the Neuropsychiatric Unit of Catania University and 200 age-matched neurologically intact HC children were recruited from local schools. Diagnoses of enuresis and other clinical conditions were made in accordance with the ICSS criteria by an experienced child neurologist. The inclusion criteria were a normal IQ and the absence of other pathological clinical conditions such as diabetes or kidney malformation. The exclusion criteria were failure to complete the initial evaluation or clinical/diagnostic procedures, inability (because of young age) to complete study questionnaires, and severe neurological or physical impairment. The study protocol was approved by the local ethics committee, and all participants provided written informed consent prior to participation.

Procedures

An outpatient medical history was obtained from child participants and their parents with a focus on neuropsychiatric disorders, psychomotor development, toilet training, urinary habits/enuresis, and sleep habits. Moreover, all participants underwent a basic physical examination as well as a kidney and bladder ultrasound examination. Venous blood and urine samples were gathered in order to exclude the possibility of organic disorders such as diabetes, antidiuretic hormone deficiency, or urinary tract infection. A fasting blood test was also performed and included a full blood count and analyses of glucose, glycated hemoglobin, azotemia, creatinine, urea, electrolytes, C-reactive protein, and the erythrocyte sedimentation rate.

During the study, child participants and their parents were asked to keep a diary (3 days per month) of nicturia, urinary incontinence, urinary frequency and volumes, and daily fluid intake. Participants (with parental assistance if needed) also completed two diaries according to the practical consensus guidelines for the management of enuresis: a daytime diary and a diary of NE and nocturnal polyuria for 14 consecutive nights [12].

Assessments

All patients and control subjects were assessed using the following instruments: the *Wechsler Intelligence Scale for Children*, 3rd edition (WISC-III) [13], Youth Quality of Life Instrument-Research Version (YQOL-R) [14], Multidimensional Anxiety Scale for Children (MASC) [15], Child Depression Inventory (CDI) [16], Conners' ADHD/DSMV-IV Scale (CADS) [17], Child Behavior Checklist (CBCL) [18], Yale Global Tic Severity Rating Scale (YGTSS) [19], and Children's Yale—Brown Obsessive Compulsive Scale (CY-BOCS) [20]. All subjects (patients and controls) underwent the complete evaluation.

The WISC III is a validated and widely used tool for IQ assessment. The MASC and CDI were used to assess anxiety and depression, the CADS provided an indication of symptoms related to ADHD, and the CBCL was used to assess a range of emotional and behavioral difficulties. Finally, the YGTSS was used to measure the presence and severity of tics and the CY-BOCS was used to assess symptoms related to obsessive-compulsive disorder (OCD). Of note, HC children were defined as individuals with no chronic or psychiatric disease that had scores <10 on the CADS and normal results on the CBCL.

Statistical analysis

The Student t test was used to compare behavioral and cognitive characteristics between groups. A p value ≤ 0.01 was considered to indicate statistical significance.

Results

Participant demographics

Demographic information is summarized in Table 1. A total of 200 NE patients (122 males and 78 females; mean age, 11.5 $\pm$ 3.9 years; age range, 8—15 years) and 200 HC subjects (131 males and 69 females; mean age, 11.9 $\pm$ 2.5

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Table 1 Demographic characteristics.

	NE ($n = 200$)	HCs ($n = 200$)	p
Sex (males)	122	131	0.406
Mean age	11.5 (3.9)	11.9 (2.5)	0.222
Familial history of NE	138	24	<0.000*

Note. Data are represented as the mean (standard deviation). HCs = healthy control children; NE = nocturnal enuresis.
*$p \leq 0.01$ is significant.

years; age range, 8–15 years) were included in the final analysis. Age and gender proportions were not significantly between groups. In the NE group, 138 subjects (69%) had a familial history of NE, compared to 24 subjects (12%) in the HC group ($p < 0.01$).

Behavioral evaluations

CBCL scores

The NE group demonstrated significantly higher total, internalizing, withdrawn, somatic complaint, anxious/depressed, and attention problems scores compared to the HC group ($p < 0.01$ for all comparisons; Tables 2 and 3). Alternatively, externalizing social problems, thought problems, and aggressive behavior scores were not statistically different between groups. Lastly, the HC group demonstrated a significantly higher delinquent behavior score than the NE group ($p = 0.012$; Table 3). Finally, no statistically significant sex differences were found.

CADS scores

CADS scores were significantly higher in the NE group than the HC group ($p < 0.01$; Table 2). In NE group, males presented statistically significant higher scores than females ($p = 0.002$).

Affective and anxiety symptoms

MASC scores

MASC anxiety symptom scores were significantly higher in the NE group than the HC group ($p < 0.01$; Table 2). In NE group, females presented statistically significant higher scores than males ($p = 0.000$).

Table 2 Comparison between nocturnal enuresis patients and healthy control subjects.

	NE ($n = 200$)	HCs ($n = 200$)	p
CDI	10.3 (6.1)	6.8 (5.1)	0.000*
MASC	52.9 (8.3)	40.9 (12.7)	0.000*
YGTSS	14.8 (7.7)	2.3 (2.7)	0.000*
C-YBOCS	8.4 (6.2)	3.1 (5.1)	0.000*
CADS	25.9 (14.7)	10.2 (9.9)	0.000*
CBCL	79.6 (25.7)	28.3 (24.6)	0.000*

Note. Data are represented as the mean (standard deviation). C-YBOCS = Children Yale–Brown Obsessive Compulsive Scale; CBCL = Child Behavior Checklist; CDI = Child Depression Inventory; HCs = healthy control children; MASC = Multidimensional Anxiety for Children; NE = nocturnal enuresis.
*$p \leq 0.01$ is significant.

Table 3 Child behavior checklist scores in nocturnal enuresis patients and healthy control subjects.

	NE ($n = 200$)	HCs ($n = 200$)	p
Total	79.6 (25.7)	28.3 (24.6)	0.000*
Internalizing	50.5 (8.9)	13.6 (5.7)	0.000*
Externalizing	6.7 (3.8)	6.5 (2.9)	0.554
Withdrawn	15.2 (2.3)	3.7 (2.2)	0.000*
Somatic complaint	14.8 (4.6)	4.3 (5.1)	0.000*
Anxious/depressed	20 (3.3)	5.6 (2.8)	0.000*
Social problems	2.1 (0.9)	1.9 (1.2)	0.060
Thought problems	1.8 (0.7)	1.7 (0.9)	0.215
Attention problems	18 (1.1)	4 (1.6)	0.000*
Delinquent behavior	3.5 (2.8)	4.1 (1.9)	0.012
Aggressive behavior	2.9 (1.1)	3 (1.2)	0.239

Note. Data are represented as the mean (standard deviation). CBCL = Child Behavior Checklist; HCs = healthy control children; NE = nocturnal enuresis.
*$p \leq 0.01$ is significant.

CDI scores

CDI depressive symptom scores were significantly higher in the NE group than the HC group ($p < 0.001$; Table 2). In NE group, females presented statistically significant higher scores than males ($p = 0.004$).

Tic disorders

YGTSS scores were significantly higher in the NE group than the HC group ($p < 0.01$). Specifically, 104 subjects (52%) in the NE group presented with tics or Tourette's syndrome, compared with 51 subjects (25.5%) in the HC group (Table 2). In NE group, males presented statistically significant higher scores than females ($p = 0.000$).

OCD

CY-BOCS scores were significantly higher in the NE group than in the HC group ($p < 0.01$). Specifically, 24 subjects (12%) in the NE group presented with OCD (CY-BOCS score >14), compared with seven subjects (3.5%) in the HC group (Table 2). In NE group, females presented statistically significant higher scores than males ($p < 0.000$).

Quality of life

Quality of life scores were significantly lower in the NE group than the HC group; specifically, between-group differences were significant in the relationship and self domains ($p > 0.01$ for both comparisons; Table 4). In the NE group, no statistically significant differences were found between male and female in the relationship domain; with regards to the "self" domain females presented statistically significant lower scores with males.

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Table 4 Quality of life scores in nocturnal enuresis patients and healthy control subjects.

	NE (n = 200)	HC (n = 200)	p
QOL TOT	317.1 (53.6)	320.0 (47.7)	0.298
QOL SELF	83.6 (23.1)	101.2 (20.0)	0.000*
QOL REL	83.5 (33.3)	114.7 (22.0)	0.000*
QOL ENV	82.6 (18.0)	83.2 (11.4)	0.690
QOL GEN	26.4 (4.6)	25.7 (5.8)	0.181

Note. Data are represented as the mean (standard deviation). ENV = environment; GEN = general; HCs = healthy control children; NE = nocturnal enuresis; QOL = quality of life; REL = relationship; TOT = total.
*$p \leq 0.01$ is significant.

Discussion

The present study is the first to evaluate the presence of different neuropsychiatric comorbidities in children with primary monosymptomatic NE as diagnosed according to the new ICCS criteria. An important finding was that neuropsychiatric conditions were more prevalent in NE patients than in age-matched HC children. Females are more affected by mood and anxiety problems and males by tic disorders and ADHD, as largely reported in previous studies [21–23]. In agreement with our data, previous studies have reported associations between enuresis and ADHD [4,5], oppositional defiant disorder [7], conduct disorders [8], and impaired quality of life [10]. However, to the best of our knowledge, this is the first study to report associations between enuresis and OCD as well as tic disorder, and is the first to describe the comparative psychopathological profiles of 200 children with enuresis and 200 matched HC children.

Our study identified several demographic differences between the NE and HC groups. With regard to familial history, our data showed that children affected by NE were more likely to have relatives with NE (69%) than the HC children (12%). These data are in agreement with a previous report indicating that NE is genetically determined in approximately 75% of affected children [24]. With regard to behavior, the NE group demonstrated significantly higher total CBCL scores and higher internalizing, withdrawn, somatic complaint, anxious/depressed, and attention problems subscores compared to the HC group. No differences were identified in the externalizing, social problems, thought problems, or aggressive behavior subscores. Finally, and surprisingly, the HC group demonstrated a significantly higher delinquent behavior subscore than the NE group. Von Gontard et al. [3] evaluated CBCL scores in 1001 children and adolescents affected by functional incontinence and concluded that children with incontinence exhibited high rates of comorbid behavioral symptoms in every subscore domain. Differences between this study and the present study are likely related to differences in the age ranges studied: Von Gontard and colleagues studied an age range of 2–18.3 years (mean age, 8.5 ± 3 years), which may better represent adolescents than the age range studied in our research (8–15 years).

In line with our CBCL results, we also found that CADS scores were higher in NE patients than in HC children, suggesting that ADHD was more prevalent in children with NE. This finding is consistent with several studies reporting a higher incidence of ADHD in children with enuresis [6,9]. In the Avon Longitudinal Study of Parents and Children, the overall prevalence of ADHD in a large sample of enuretic children was 17.6% (vs. 11.9% in continent children) [25]. Based on these results, the presence of ADHD, tic disorders, or OCD in patients with NE could be related to abnormal central nervous system processes (with particular regard to the processing of the emotions) [26] and aberrant brain activation during response inhibition leading to an inability to suppress inappropriate responses [27].

We also found that NE children had higher depressive and anxiety symptoms and lower quality of life than HC children. Koca et al. [28] reported a higher prevalence of depression in children with NE than in HC children. Moreover Al-Zaben et al. [29] reported that punishment for bedwetting was associated with a greater severity of depression in children with NE. However, there is no consensus in the literature regarding the presence of anxiety in enuretic children. Koca et al. [28] reported that enuretic children exhibited fewer anxiety symptoms compared to HC subjects, whereas Phung et al. [30] reported that 10% of children with primary NE presented with anxiety. Additional work is required to clarify the factors influencing the manifestation of anxiety symptoms in NE patients. With regard to quality of life, our result is in line with previous literature [9,10]. Lower scores in the relationship and self domains suggest that children with NE suffer losses in self-esteem or confidence and interpersonal skills. It is clear and well accepted that bedwetting, especially if persistent after 10 years of age [30], can be responsible for clinical and subclinical internalization problems [10].

Our paper has highlighted the importance of neuropsychiatric disorders in patients affected by NE and focused on an important matter: are NE and neuropsychiatric disease comorbidities or coexisting conditions?

Recently it has been suggested that patients affected by NE presented abnormal neural responses to emotional stimuli [31], pathologically increased excitability, reduced inhibitory processing in the motor cortex [32], and abnormal cerebral control network of micturition with metabolism abnormalities in the prefrontal cortex and the pons [33]. Similar features were reported in some neuropsychiatric condition such as ADHD, tic disorders, and OCD; it is largely reported that these diseases presented impaired inhibitory control in the motor cortex [34,35].

In the context of our study findings, it is peculiar and interesting that NE sample presented all comorbidities related to abnormal excitability and impaired inhibitory control in the motor cortex, but this is just an association study and more research is needed to identify the possible causality and the hypothesized relationship.

The present study had some limitations. First, our clinic is a tertiary expert clinic, such that our cohort may not have been representative of all individuals with NE. Second, we did not take into account the effect of medications

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on various symptoms, which may be a fruitful area of exploration in future studies.

Conclusion

In conclusion, our results are in agreement with the practical consensus guidelines for the management of enuresis [12]: clinicians should not underestimate the effects of enuresis on psychosocial development. Childhood NE should be managed carefully and comprehensively to identify behavioral problems in the future that could be associated to the disorder.

Conflicts of interest

None.

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Largo Gemelli 1 - Aula Magna Cripta

IL CONVEGNO

Il disturbo da Deficit d'Attenzione e Iperattività (ADHD), in quanto disturbo del neurosviluppo, fino a poco tempo fa era ritenuto esclusivo dell'età evolutiva. Invece si tratta di una patologia che "come un filo rosso attraversa tutte le fasi della vita" (fonte: OMS).

Il disturbo è caratterizzata da una sintomatologia multiforme riconducibile a tre aree principali: l'attenzione, l'impulsività e l'iperattività. Se non è riconosciuto e curato adeguatamente nell'infanzia o nell'adolescenza, la sua sintomatologia persiste nell'età adulta e causa alla persona una serie di condizioni psichiatriche che influenzano negativamente il suo funzionamento sociale, lavorativo, affettivo e familiare. Queste condizioni hanno poi un severo impatto sulla vita del paziente e della sua famiglia.
Le persone con ADHD spesso non raggiungono un livello scolastico o accademico adeguato alle loro reali capacità, tendono più facilmente alle dipendenze, all'abuso dal alcool, nicotina o altre sostanze. Le persone con ADHD sono impulsive e faticano a controllare le loro emozioni: spesso assumono atteggiamenti aggressivi che possono condurre a condotte pericolose o addirittura antisociali e/o illegali.
Il convegno propone una serie di interventi che mirano a chiarire e ad illustrare le caratteristiche del disturbo ADHD nell'età adulta: sintomatologia, compromissioni funzionali, iter diagnostico, terapie e aspetti sanitario-burocratici (es. transizione dai servizi di NPI a quelli di Psichiatria).

L'evento è rivolto a medici e a professionisti della salute mentale dell'adulto. E' indirizzato altresì a studenti di medicina, psicologia e psichiatria, figure educative e del mondo dell'assistenza sociale.

Ingresso gratuito, iscrizione obbligatorio via mail a ***referente.milano@aifa.it***, entro il 18 marzo con l'apposito modulo precisando la partecipazione o meno ai workshop.

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PROGRAMMA CONVEGNO 25 MARZO 2017

MATTINO

Ore 8,30 registrazione dei partecipanti

Chairman *Cristiano Termine*

Ore 9,00 **Saluti e presentazione Aifa Onlus**
Le famiglie chiedono aiuto
Astrid Gollner

Ore 9,30 **L'ADHD nell'infanzia – breve introduzione sul disturbo nell'età infantile**
Cristiano Termine

Ore 10,00 **"Io ho l'ADHD" – testimonianza di un adulto**
Jasmine Rizzi

Ore 10,30 **Clinica dell'ADHD nell'adulto**
Marco Uccello

Ore 11,00 Pausa – coffee break

Ore 11,20 **Transizione dalla Neuropsichiatria alla Psichiatria**
Chiara Gori

Ore 11,40 **Il protocollo diagnostico**
Francesca Sgroi

Ore 12,20 **Il trattamento farmacologico**
Nicoletta Brunello

Ore 13,00 **Universitari con ADHD: indagine sulle difficoltà di studio ed organizzative**
Progetto promosso da AIDAI Lombardia in collaborazione con l'Università Cattolica di Milano e AIFA Onlus Lombardia
Elisa Zugno

Ore 13,15 - 14,30 Pausa pranzo

Sessione poster sulla ricerca condotta da AIDAI in collaborazione con Università Cattolica e AIFA sulle difficoltà dello studente universitario con ADHD

POMERIGGIO

Ore 14,30 **Il trattamento non farmacologico – la terapia multimodale**
Sonia Holzer e Ylenia Endrizzi

Ore 15,15 Workshop
Valutazione diagnostica ed uso dei più diffusi strumenti testali (es. DIVA)
Francesca Sgroi

Ore 16,15 Workshop
La valutazione clinica: diagnosi differenziale ed eventuali comorbilità psichiche
Giovanni Migliarese

Ore 17,15 Dibattito

ADHD: LA DIAGNOSI NELL'ADULTO
Disturbo da Deficit di Attenzione e Iperattività
25 marzo 2017
Università Cattolica del Sacro Cuore

SCHEDA DI ISCRIZIONE

Il convegno è gratuito

Alla fine del convegno, l'organizzatore (A.I.F.A Onlus Lombardia) rilascerà un attestato di partecipazione. Per ottenerlo è necessario inviare la presente scheda di iscrizione specificando anche la partecipazione o meno ai due workshop del pomeriggio

Cognome …… Nome……

Professione…… Ente/altro……..

E-mail…… Tel……

Partecipo ai workshop "Valutazione diagnostica" e "Valutazione clinica" ☐ SI ☐ NO

Usufruisco del servizio mensa (€ 10) ☐ SI ☐ NO

Data …… Firma……

Inviare per e-mail a referente.milano@aifa.it entro 18/03/2017

Informazioni: referente.milano@aifa.it **tel 338 4145662 e a** referente.lombardia@aifa.it **tel 338 5921605**

INFORMATIVA

La informiamo ai sensi dell'art.13 del d.lgs. n. 196 del 30 giugno 2003 "Codice in materia di protezione dei dati personali"
che i dati personali da Lei forniti potranno formare oggetto di trattamento, nel rispetto della normativa sopra citata e degli obblighi di riservatezza cui è ispirata la attività della nostra Associazione. In particolare tali dati potranno essere raccolti su supporto cartaceo, registrati su supporti elettronici, estratti e riprodotti per l'invio di comunicazioni postali, comunicati alla Sede e ivi custoditi. Il conferimento dei dati personali è facoltativo ma consente l'identificazione dell'interessato per un periodo di tempo non superiore a quello necessario agli scopi per i quali essi sono stati raccolti o successivamente trattati. In relazione al trattamento dei suoi dati personali Ella potrà esercitare i diritti di cui all'art. 7 del d.lgs. n. 196 del 30 giugno 2003. L'A.I.F.A Onlus Lombardia (Associazione Italiana Famiglie ADHD) ha sede a 21046 Malnate, in Via Sabotino,4.
Legge completa:http://www.garanteprivacy.it/garante/doc.jsp?ID=1311248

CONSENSO

Il sottoscritto autorizza A.I.F.A. Onlus Lombardia al trattamento dei dati personali per la partecipazione al Convegno, per ricevere informazioni mediante posta, telefono, posta elettronica e dichiara di avere ricevuto le informazioni di cui all'art. 13 del D.lgs. 196/2003 in particolare riguardo ai diritti da me riconosciuti dalla legge ex art. 7 D.lgs. 196/2003, acconsente al trattamento dei miei dati con le modalità e per le finalità indicate nella informativa stessa, comunque strettamente connesse e strumentali a rapporti con l'A.I.F.A. Onlus.

Data…… Firma……

A.I.F.A. Onlus LOMBARDIA Associazione Italiana Famiglie ADHD
C.F. 95068220128
Sede legale: Via Sabotino 4 21046 Malnate (Va)
www.aifaonlus.it e-mail: referente.lombardia@aifa.it

Per ricevere la newsletter iscriversi al seguente indirizzo:
http://www.adhd.marionegri.it/index.php/newsletter/iscrizione-newsletter

Iniziativa nell'ambito del Progetto di Neuropsichiatria dell'Infanzia e dell'Adolescenza
(Delibera n. 406 - 2014 del 04/06/2014 Progetti NPI)
Il Progetto è realizzato con il contributo, parziale, della Regione Lombardia
(in attuazione della D.G. sanità n. 3798 del 08/05/2014, n. 778 del 05/02/2015 e n. 5954 del 05/12/2016) Capofila Progetto: UONPIA Azienda Ospedaliera "Spedali Civili di Brescia" "*Percorsi diagnostico-terapeutici per l'ADHD*".

IRCCS ISTITUTO DI RICERCHE FARMACOLOGICHE MARIO NEGRI
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