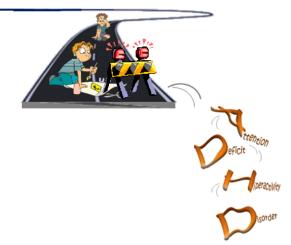
# **NEWSLETTER**





# INDICE:

1. Dalle banche dati bibliografiche

pag. 2



# BIBLIOGRAFIA ADHD MARZO 2018

Acta Neuropsychol. 2017;15:283-301.

MANAGEMENT OF ATTENTION DEFICIT AND FINE MOTOR INCOORDINATION OF PRIMARY SCHOOL GOING ADHD (INATTENTIVE TYPE) CHILDREN.

Khan NA, Jahan M, Kanchan A, et al.

**Background**: Children with Attention Deficit/Hyperactive Disorder (ADHD) have a wide range of neuropsychological deficits including attention, memory, and executive functioning. The study was targeted to use a neuropsychological approach in remediating attention and fine motor training or the incoordination of children with ADHD- Inattentive type (IA).

**Material/ Methods**: A total of 20 primary school children fulfilling the criteria of ADHD- IA type were selected from different schools in Mysuru, India. Neuropsychological deficits were assessed using appropriate tools. Children in the experimental group were given attention and fine motor training for 3 months. A post test was conducted after 3 months training. The maintenance effect of therapy was studied until the completion of 1 year.

**Results**: Results revealed that attention fine motor training was effective in improving focused and selective attention, working memory, new learning ability, visual fluency and fine motor training incoordination.

**Conclusions**: It can be concluded that a neuropsychological rehabilitation is effective in remediating the deficits faced by children with ADHD-IA

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.

Actas Esp Psiguiatr. 2017 Jan;45:12-20.

SLEEP STUDY IN DISRUPTIVE MOOD DYSREGULATION DISORDER AND BIPOLAR CHILDREN.

Estrada-Prat X, Alvarez-Guerrico I, Bleda-Hernandez MJ, et al.

**INTRODUCTION**: Decreased need for sleep has been proposed as a core symptom of mania and it has been associated with the pathogenesis of Bipolar Disorder. The emergence of Disruptive Mood Dysregulation Disorder (DMDD) as a new diagnostic has been controversial and much has been speculated about its relationship with the bipolar spectrum. REM sleep fragmentation could be a biomarker of affective disorders and it would help us to differentiate them from other disorders.

**METHOD**: Polysomnographic cross-sectional study of children with DMDD, bipolar disorder and Attention Deficit Hyperactivity Disorder (ADHD). All participants underwent a psychiatric semi-structured interview to obtain the diagnosis, comorbidities and primary sleep disorders. DMDD's sample was performed following DSM5 criteria.

**GOALS**: Perform polysomnography in a sample of bipolar, DMDD and ADHD children and compare their profiles to provide more evidence about the differences or similarities between bipolar disorder and DMDD. **RESULTS**: Bipolar group had the highest REM density values while ADHD had the lowest. REM density was not statiscally different between bipolar phenotypes. REM density was associated with antidepressant treatment, episodes of REM and their interaction. REM latency was associated with antipsychotic treatment and school performance. Bipolar patients had higher scores on the depression scale than DMDD and ADHD groups.

**CONCLUSIONS**: No significant differences between the two compared affective disorders were found. However there were differences in REM density between bipolar and ADHD groups. REM sleep study could provide a new theoretical framework to better understand the pathogenesis of pediatric bipolar disorder

.....

Adicciones. 2016 Oct;29:125-33.

ADOLESCENTS WITH INTERNET GAMING DISORDER (IGD): PROFILES AND TREATMENT RESPONSE.

Martin-Fernandez M, Matali JL, Garcia-Sanchez S, et al.

Demand for treatment for problems related to the use of video games have increased significantly in adolescents. Most cases have a comorbid mental disorder that jeopardises both pathologies. The aim of this study is to describe profiles of adolescents with Internet Gaming Disorder (IGD) according to comorbidity and analyze treatment response at 3 and 6 months. A sample of 86 patients which consulted in the Addictive Behavior Unit of a hospital was assessed with diagnostic criteria for IGD, the interview K-SADS-PL for mental disorders and the Clinical Global Impression (CGI) to treatment progress. Of the initial sample, 68,6% (n = 59) met diagnostic criteria for IGD. Of these, the 45,76% matched an internalizing profile, presenting comorbidity with Mood Disorders (44,4%), Anxiety Disorders (44,4%) and Personality Disorders (11,1%). The externalizing profile would comprise 52,54% of the sample presenting Disruptive Behavior Disorder (48,4%=, ADHD (29%) and Disruptive Behavior Disorders not otherwise specified (22,6%). Unlike externalizing, the internalizing patients had a family history of psychiatric problems (63%), difficulties in social relationships (77,8%) and seemed to use video games preferably to escape discomfort (66,7%). After 3 months the externalizing profile showed improvements. Comorbid disorders allow the discrimination of two IGD profiles in adolescents and these could influence treatment response. Therefore, it is important to assess comorbidities to design a more accurate intervention focused on the specificities of each profile

.....

Alcohol Alcohol. 2015;50:i42.

THE ASSOCIATION OF ATTENTION DEFICIT HYPERACTIVITY DISORDER, SUBSTANCE USE AND THE MOTIVATION TO CONSUME ALCOHOL AND NICOTINE IN YOUNG AUSTRIAN MALES.

Riegler A, Lesch O.

The abuse of alcohol, nicotine and illicit drugs often occurs together with other disorders and the causes are very complex. One disorder that is increasingly linked to the abuse of psychoactive substances is attention deficit hyperactivity disorder (ADHD). Substance abuse seems to be highly prevalent in adolescents with

Newsletter – ADHD marzo 2018

ADHD, conversely there is also a growing number of studies that report a high prevalence of ADHD in patients treated for the abuse or dependence of alcohol, nicotine or illicit drugs. Aim. The aim of the study was to investigate the association between ADHD and substance use in a representative sample of 18-year-old males. Another focus was to assess the role of ADHD in the motivation to consume alcohol or nicotine. Screening instruments: The 25-item Wender Utah Rating Scale and the ADHD checklist were used to assess ADHD symptomatology. The CAGE questionnaire was used to test for alcohol misuse and dependence and the Heavy Smoking Index (HSI) to test for nicotine dependence. Findings. The number of ADHD symptoms was positively related to the CAGE score, the severity of nicotine dependence and to the use of illicit drugs. ADHD symptomatology was also associated with different drinking and smoking motives. Conclusion: The results underline the increased vulnerability of 18-year old males with elevated symptom severity of ADHD for smoking, drinking and illicit drug use

.....

Am J Occup Ther. 2018 Jan;72:7201190040p1-7201190040p11.

SPECIFIC SENSORY TECHNIQUES AND SENSORY ENVIRONMENTAL MODIFICATIONS FOR CHILDREN AND YOUTH WITH SENSORY INTEGRATION DIFFICULTIES: A SYSTEMATIC REVIEW.

#### Bodison SC, Parham LD.

This systematic review examined the effectiveness of specific sensory techniques and sensory environmental modifications to improve participation of children with sensory integration (SI) difficulties. Abstracts of 11,436 articles published between January 2007 and May 2015 were examined. Studies were included if designs reflected high levels of evidence, participants demonstrated SI difficulties, and outcome measures addressed function or participation. Eight studies met inclusion criteria. Seven studies evaluated effects of specific sensory techniques for children with autism spectrum disorder (ASD) or attention deficit hyperactivity disorder: Qigong massage, weighted vests, slow swinging, and incorporation of multisensory activities into preschool routines. One study of sensory environmental modifications examined adaptations to a dental clinic for children with ASD. Strong evidence supported Qigong massage, moderate evidence supported sensory modifications to the dental care environment, and limited evidence supported weighted vests. The evidence is insufficient to draw conclusions regarding slow linear swinging and incorporation of multisensory activities into preschool settings

.....

Am J Perinatol. 2016 May:33:540-46.

PREDICTIVE CAPABILITIES OF NEUROBEHAVIORAL DIAGNOSTICS IN EARLY CHILDHOOD.

#### Abramova O.

Modern world experiences annual increase in the number of children born with neurological problems, which in the future may stipulate the development of their neurobehavioral and neuropsychological aberrations. Specific functional features of a child's brain development depend on many factors, but there is a strong need for early clinical and psychological identification of a child's development with a view to elaborate preventive measures, which are often more effective than the treatment or correction of dysfunction, already complicated by compensatory bonds. One should note that despite a high interest in the possibility of predicting the future development of the child in the early ontogenesis, few studies have so far been devoted to the search for indicators that could be meaningful for neuropsychology, neurology, and educational, special, and clinical psychology

.....

Anadolu Psikiyatr Derg. 2016;17:8.

EFFICACY OF PHARMACOTHERAPY AND BEHAVIOR TREATMENT ON ATTENTION-DEFICIT HYPERACTIVE CHILDREN.

#### Chinaveh M.

**Introduction**: Attention-deficit/hyperactive disorder (ADHD) is a prevalent disorder of child onset, characterized by attention dysfunction, impulsivity and hyperactivity. Indeed more studies have been

published on ADHD and its variations than other disorders of childhood, is the continuing gaps in our knowledge about efficacy of treatments on ADHD.

**Objective**: This study has compared the effective of 3 interventions on ADHD symptoms, attention span and academic performance in children with ADHD.

**Methods**: A total of 197 children who were 7 to 10 years of age and had ADHD as defined by the Diagnostic and Statistical Manual of Mental Disorders, 5th edition, were assigned to 6 months of medication management (Ritalin followed by monthly visits); behavioral treatment, the two combined; and control group. Child Attention Deficit Disorder (ADD/ADHD) Test was used to assess attention span; and the Academic Performance Index (API) measured academic performance and progress of individual schools. Data were analyzed through ANOVA.

**Results**: For most ADHD symptoms, children in the combined treatment and medication management groups showed significantly greater improvement than that given behavioral treatment. In addition, combined and medication management treatments did not differ significantly on any ADHD symptoms, but Comb intervention was substantially superior to attention span and academic performance; Ritalin intervention for attention span; and behavioral treatment for academic performance

.....

Ann Epidemiol. 2017 Jul;27:448-53.

AUTISM SPECTRUM DISORDERS AND THEIR TREATMENT WITH PSYCHOTROPIC MEDICATIONS IN A NATIONALLY REPRESENTATIVE OUTPATIENT SAMPLE: 1994-2009.

Kamimura-Nishimura K, Froehlich T, Chirdkiatgumchai V, et al.

**PURPOSE**: No prior studies have assessed change in health care provider-coded rates of Autism spectrum disorder (ASD) diagnoses over time, and few have investigated sociodemographic factors associated with having an ASD diagnosis, having behavioral conditions comorbid with ASD, or using psychotropic medications for this group.

**METHODS**: We used data from the 1994-2009 National (Hospital) Ambulatory Medical Care Surveys for children aged 2-18 years (n = 158,488).

**RESULTS**: Rates of visits with coded-ASD per 100 outpatient medical visits increased from 0.04% to 0.82% from 1994 to 2009. Factors associated with an ASD diagnosis included male gender, lack of private insurance, white race, and later study period. The most frequent comorbid behavioral diagnoses were ADHD, anxiety, disruptive behavior, and mood disorders. Older age was linked to an increased likelihood of having a comorbid behavioral diagnosis and using psychotropic medications. Geographic region was also associated with having a comorbid behavioral diagnosis, and psychotropic use was linked to have a behavioral comorbidity. Comorbidities with the highest rates of psychotropic use were ADHD, mood, and anxiety disorders.

**CONCLUSIONS**: Pediatric outpatient visits with an ASD diagnosis have increased dramatically from 1994 to 2009. Further study is needed to determine the reasons for the observed sociodemographic disparities in ASD diagnosis

.....

Ann Gen Psychiatry, 2018:17.

PARENT-CHILD INTERACTION THERAPY (PCIT) FOR YOUNG CHILDREN WITH ATTENTION-DEFICIT HYPERACTIVITY DISORDER (ADHD) IN JAPAN.

Hosogane N, Kodaira M, Kihara N, et al.

Early intervention for preschoolers with Attention-Deficit Hyperactivity Disorder (ADHD) is important considering the impact on their prognosis. Parent-Child Interaction Therapy (PCIT) is a psychotherapy treatment for the parent-child dyad and has been shown to be effective for children with disruptive behaviors. We present the treatment course of PCIT for two Japanese children with ADHD. Case 1 is a 2-year-old female child with hyperactivity and aggressiveness. Case 2 is a 4-year-old male child with restlessness and

intolerability to daily events. For both cases, PCIT was effective in improving the problematic behaviors. PCIT may serve as a treatment option for Japanese children with ADHD

.....

Ann Gen Psychiatry. 2018 Feb;17.

PARENT—CHILD INTERACTION THERAPY (PCIT) FOR YOUNG CHILDREN WITH ATTENTION-DEFICIT HYPERACTIVITY DISORDER (ADHD) IN JAPAN.

#### Hosogane N, Kodaira M, Kihara N, et al.

Early intervention for preschoolers with Attention-Deficit Hyperactivity Disorder (ADHD) is important considering the impact on their prognosis. Parent–Child Interaction Therapy (PCIT) is a psychotherapy treatment for the parent–child dyad and has been shown to be effective for children with disruptive behaviors. We present the treatment course of PCIT for two Japanese children with ADHD. Case 1 is a 2-year-old female child with hyperactivity and aggressiveness. Case 2 is a 4-year-old male child with restlessness and intolerability to daily events. For both cases, PCIT was effective in improving the problematic behaviors. PCIT may serve as a treatment option for Japanese children with ADHD

.....

Ann Pharmacother. 2018.

THE IMPACT OF VITAMIN D SUPPLEMENTATION ON ATTENTION-DEFICIT HYPERACTIVITY DISORDER IN CHILDREN.

Elshorbagy HH, Barseem NF, Abdelghani WE, et al.

**Background**: The role of nutrients and dietary factors in attention-deficit hyperactivity disorder (ADHD) remains unclear.

**Objectives**: The primary objective was to evaluate the serum vitamin D level in children with a diagnosis of ADHD. The secondary objective was to detect the effect of vitamin D supplementation on cognitive function in those with vitamin D deficiency.

**Methods**: A total of 50 children with ADHD and 40 healthy controls were included in the study. We measured the serum level of vitamin D. Patients with vitamin D deficiency were subdivided into 2 groups: one with vitamin D supplementation and the other without vitamin D supplementation. Further assessment and follow-up of children with ADHD was done. The Wisconsin Card Sorting Test, Conners Parent Rating Scale, and Wechsler Intelligence Scale for Children were performed at baseline and follow-up in all cohorts with an ADHD diagnosis.

**Results**: The diagnosis of vitamin D deficiency was significantly greater in children with ADHD compared with the control group (P < 0.05). Children with ADHD had significantly (P = 0.0009) lower values of serum vitamin D (17.23  $\pm$  8.98) than the control group (31.47  $\pm$  14.42). The group receiving vitamin D supplementation demonstrated improvement in cognitive function in the conceptual level, inattention, opposition, hyperactivity, and impulsivity domains.

Conclusion: Vitamin D supplementation in children with ADHD may improve cognitive function

Arch Pediatr. 2018.

ALL YOU NEED TO KNOW ABOUT METHYLPHENIDATE (AND DARED NOT ASK).

#### Zimmer L, Fourneret P.

Methylphenidate (MPH) remains the only accessible psychostimulant used in France in the attention and behavior disturbances of attention deficit disorder with or without hyperactivity (ADHD). Its prescription has been extended during the past decade to other neurodevelopmental disorders in children and adolescents, also associated with a deficit of attentional resources or, more broadly, fragility of executive functions. Despite its efficiency, validated by more than 400 randomized controlled and double-blind studies, and the good tolerance of MPH in these indications, this treatment remains limited in France because of many fears and other prejudices on the part of medical practitioners and/or families. This article, resulting from the complementary viewpoints of a psychiatrist and a neuropharmacologist, is not intended to advocate MPH

but to present, in a concise and nuanced manner, the approved scientific data justifying and framing this prescription

.....

Arch Dis Child. 2017;102.

PRENATAL EXPOSURE TO ACETAMIN-OPHEN AND RISK FOR ATTENTION DEFI-CIT DISORDER (ADHD): A SYSTEMATIC REVIEW AND META ANALYSIS.

Reem, Reif, Levine, et al.

**Background** Acetaminophen is the most commonly used analgesic and antipyretic medication during pregnancy. Recent epidemiological studies have suggested a possible association between acetaminophen exposure in-utero and impaired paediatric neurological develop-ment, including hyperactive attention deficit (ADHD) and related disorders.

**Methods** We conducted a systematic-review and me-ta-analysis to evaluate the risk for ADHD in children of women exposed to acetaminophen during pregnancy. We searched MEDLINE and EMBASE up to January 2017. We used meta-regression analysis to evaluate factors that may moderate this association. Reports of cohorts were pooled using random-effects models.

**Results** Six cohort studies met our inclusion criteria. Among 76 146 mothers who reported acetaminophen use during pregnancy, acetaminophen was associated with an increased risk for ADHD (RR=1.33, 95% CI: 1.19-1.47, I2=77%), hyperactivity symptoms (RR=1.24, 95% CI: 1.02-1.46, I2=95%), and conduct disorders (RR=1.28; 95% CI, 1.05-1.52, I2=93%). Using meta-regression, we found that the association was greater and heterogeneity re-duced as child's age at diagnosis increased (+!=0.045, p=0.035, heterogeneity accounted for (R2)=65.98%).

**Conclusion** This meta-analysis suggests that maternal acetaminophen use during pregnancy is associated with a higher risk for ADHD or related disorders. However, there is evidence of significant heterogeneity in the observed effect, and many of the studies suffer from significant lim-itations. These findings, together with additional recent evidence on teratogenicity of acetaminophen, warrants further investigation and consideration of public health actions

.....

Arch Neurocienc, 2017;22:30-39.

MEMORY AND ATTENTION IN PRETERM AND/OR LOW BIRTH WEIGHT IN SCHOOL CHILDREN.

González IJA, et al.

**Introduction**: in Mexico City, there is no literature or evidence of memory and attention deficits in preterm and/or low birth weight school children.

**Objective**: to determine whether there is memory and attention deficits in Mexican school children born preterm or with low birth weight or very low birth weight.

**Material & methods**: we performed a neuropsychologic test in Mexican population, we applied the ENI test to 31 preterm and/or low birth weight school children (age 8-12), we studied short term memory, long term memory (verbal and visual respectively) and also visual and hearing attention.

**Results**: the results we had were: verbal short term memory deficit was reported in 67.74% of the population, visual short term memory was reported in 61.29%; we found a deficit of verbal long term memory in 74.2%, whereas visual long term memory deficit was found in 80.64%. visual attention deficit was reported in 83.87% and hearing attention shortfall was found in 35.49%

**Conclusions**: preterm, low birth weight and very low birth weight children present a high deficit percentage in visual and hearing attention, as well as in verbal and visual long term memory and short term memory

Asian J Psychiatry. 2018;33:7-10.

FAMILIAL STUDY OF ATTENTIONAL AND BEHAVIOURAL PROBLEMS IN CHILDREN WITH DYSLEXIA AND THEIR FIRST-DEGREE RELATIVES IN INDIAN SETTING.

Sharma P, Sagar R, Pattanayak RD, et al.

**Background**: Dyslexia is one of the common problems seen in children worldwide. There is high co-morbidity of dyslexia with attentional and behaviour problems which could have familial pattern. This study aims to compare the attentional and behavioural problems in children with dyslexia and their first-degree relatives with controls.

**Methods**: This is a cross-sectional comparative study with single interview method in an out-patient setting. Formally diagnosed (ICD-10) cases of 30 children with specific reading disorder and 30 healthy matched controls and their first-degree relatives were assessed using scales in a single setting after application of inclusion and exclusion criteria.

**Results**: The children with dyslexia had significantly more problems in the domains of selective attention and behavioural problems as compared to controls and the siblings of the cases had significant problems in selective attention but not in behavioural problems. Also, no difference was seen in ADHD symptoms of parents in cases and controls.

**Conclusion**: The results from our study are keeping with most of the published literature. We expect that this study will help in laying a good foundation for further studies with stronger methodologies incorporating molecular genetics

.....

Asian J Psychiatry. 2018;33:68-73.

IMPLICATIONS OF COMORBID ADHD IN ASD INTERVENTIONS AND OUTCOME: RESULTS FROM A NATURALISTIC FOLLOW UP STUDY FROM SOUTH INDIA.

Manohar H, Kuppili PP, Kandasamy P, et al.

**Background**: Autism Spectrum Disorder (ASD) is a neurodevelopmental disorder commonly associated with Attention Deficit Hyperactivity Disorder (ADHD), the prevalence ranging from  $14\Gamma$ Çô70%. The current study attempted to assess the impact of comorbid ADHD in children with ASD, in terms of challenges in diagnosis, treatment, intervention outcomes and parental stress and coping through a naturalistic design.

**Methods**: Fifty children aged 2-6 years with ASD were recruited, assessed and followed up for six months. Twenty children were found to have comorbid ADHD. Severity of ASD and ADHD was assessed by Childhood Autism rating scale and Connor's abbreviated rating scale respectively. Parental stress and coping was assessed by Family Interview for stress and coping.

**Results**: The diagnosis of ASD was apparently obscured by ADHD symptoms in about 22% of cases, as only diagnosis of ADHD was made at the time of referral to our centre. ADHD was the most common comorbidity followed by intellectual disability and seizure disorder. About 66% of children received combination of pharmacological and behavioral interventions. Clonidine was the most common medication to be used and was well tolerated. The improvement in ADHD symptomatology showed positive correlation with improvement with ASD-specific interventions as reflected by change in severity scores. Severity of ADHD significantly also predicted parental stress and coping, and thereby engagement in ASD-specific interventions.

**Conclusion**: The current study highlights the need for screening and early diagnosis of comorbid ADHD in children with ASD and vice versa considering the management challenges. In case of multiple comorbid neurodevelopmental disorders, early interventions for one disorder can improve the outcome of the other

Aten Prim. 2015;47:5.

EXECUTIVE FUNCTIONS BEHAVIOR IN CHILDREN AND TEENAGERS DIAGNOSED WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER (ADHD).

Borges CR, Fran+ºa LE, Dos Santos DB, et al.

**Introduction**: Attention deicit hyperactivity disorder (ADHD) is one of the most common pathology in children and teenagers. ADHD is characterized by three somatic manifestations: inattention, hyperactivity and impulsivity. The Executive Functions are a set of pre-frontal cortex related functions which represents a group of skills responsible for the behavior planning and monitoring, also integrating and selecting information which enable the concepts formation. Therefore, the present study is a literature review about relations between ADHD and affected Executive Functions in diagnosed children.

**Methods**: Studies that linked hyperactivity disorder and attention deicit with executive functions, as well those with neuropsychological evaluation in children diagnosed with the disorder were conducted by a research with keywords 'ADHD' AND 'executive functions' at SciELO and Lilacs database between 2005 and 2015. Studies related to children and teenagers diagnoses were emphasized.

**Results**: ADHD seems to be a result of a complex combination of genetic, biological, environmental and social factors. It shows a prevalence of 9/1 boys when related to girls in clinical samples. For epidemiological purposes, the studied age group varies from 7 to 14 years old, also, studies have shown that about 60% to 70% of children with ADHD will hold the diagnoses to adulthood.

**Conclusions**: Studies show that ADHD patients may indicate losses on executive functions, mainly the ones related to inhibitory control, selective concentrated attention and to working memory executive center. Since it's possible to comprehend more about the children's dificulties with the knowledge about the cognitive losses obtained by this disorder, more studies on this ield are required

.....

Autism. 2016 Nov;20:963-72.

SOCIOECONOMIC STATUS AND INTELLIGENCE QUOTIENT AS PREDICTORS OF PSYCHIATRIC DISORDERS IN CHILDREN AND ADOLESCENTS WITH HIGH-FUNCTIONING AUTISM SPECTRUM DISORDER AND IN THEIR SIBLINGS.

#### Rosa M, Puig O, Lazaro L, et al.

Previous studies have shown high rates of comorbid disorders in children and adolescents with autism spectrum disorder, but failed to compare them with general population and few of them have identified predictors of comorbidity. This study compared the rates of psychiatric disorders in 50 children and adolescents with autism spectrum disorder, 24 of their siblings, 32 controls from general population and 22 of their siblings. Children and adolescent with autism spectrum disorder and their siblings had higher rates of attention deficit and hyperactivity disorder compared to controls. Lower socioeconomic status and intelligence quotient were the main risk factors. The contribution of socioeconomic status and intelligence quotient to increase the risk of developing comorbidity in autism spectrum disorder and psychopathology in their siblings deserves further study

Behav Brain Res. 2017 Jun;329:58-66.

EMG BIOFEEDBACK TRAINING IN ADULT ATTENTION-DEFICIT/HYPERACTIVITY DISORDER: AN ACTIVE (CONTROL) TRAINING?

Barth B, Mayer K, Strehl U, et al.

**OBJECTIVE**: The present study aimed at revealing neurophysiological effects induced by electromyography (EMG) based biofeedback, considered as a semi-active control condition in neurofeedback studies, in adult attention-deficit/hyperactivity disorder (ADHD) patients.

**METHODS**: 20 adult ADHD patients trained their muscle activity in the left and right supraspinatus muscle over the course of 30 EMG biofeedback sessions. Changes induced by the EMG feedback were evaluated at a clinical and neurophysiological level; additionally, the relation between changes in EEG activity recorded at the vertex over the training course and changes of symptom severity over the treatment course were assessed in order to investigate the mechanisms underlying clinical effects of EMG biofeedback.

**RESULTS**: Participants showed significant behavioral improvements on a self-rating scale. There was a significant increase in alpha power, but no significant changes in the delta frequency range; changes in the theta and beta frequency range were not significant after adjustment for multiple comparisons. No statistically significant correlation was found between changes in EEG frequency bands and changes in ADHD symptoms.

**CONCLUSIONS**: The current results assessed by means of a single-electrode EEG constitute a starting point regarding a clearer understanding of mechanisms underlying clinical effects of EMG biofeedback. Although we did not reveal systematic effects induced by EMG feedback on brain activity it remains an open question whether EMG biofeedback induces changes in brain regions or parameters we did not gather in the present study (e.g. motor cortex)

.....

Biol Psychiatry. 2017 Jul;82:17-25.

THE PSYCHOSIS SPECTRUM IN 22Q11.2 DELETION SYNDROME IS COMPARABLE TO THAT OF NONDELETED YOUTHS. Tang SX, Moore TM, Calkins ME, et al.

**BACKGROUND**: Chromosome 22q11.2 deletion syndrome (22q11DS) is a promising model for studying psychosis risk. Direct comparisons of psychosis features between 22q11DS and nondeleted (ND) individuals are limited by inconsistency and small samples. In the largest study to date, we compare 22q11DS to ND in comorbidities, functioning, cognition, and psychosis features across the full range of overall severity.

**METHODS**: ND youths (n = 150) ages 9 to 24 years were matched to 22q11DS individuals (n = 150) on age and sex, stratifying for presence of psychosis spectrum disorder. Individuals were evaluated for psychosis using the Structured Interview for Prodromal Syndromes, and for attention-deficit/hyperactivity, substance-related, and mood disorders. Differential item functioning analysis addressed whether 22q11DS differs from ND in the probability of clinically significant ratings while holding constant the overall level of psychosis.

**RESULTS**: Onset of psychosis proneness was similar among 22q11DS (mean: 11.0 years) and ND (mean: 12.1 years) individuals. Accounting for higher overall psychosis symptoms, 22q11DS participants were still more likely to manifest impaired stress tolerance, avolition, and ideational richness; ND individuals were more likely to exhibit unusual thoughts, persecutory ideas, and bizarre thinking. Cognition was impaired in 22q11DS, but it did not correlate with symptoms except ideational richness. Comorbid anxiety disorders were more likely in psychosis spectrum 22q11DS; substance-related disorders were more likely in ND. Global assessment of function was similar in 22q11DS and ND individuals, except among those with low total Structured Interview for Prodromal Syndromes scores.

**CONCLUSIONS**: Individuals with 22q11DS share overarching similarities with ND individuals in psychosis symptoms and age of onset for psychosis proneness; this continues to support the 22q11DS model as a valuable window into mechanisms contributing to psychosis

.....

Biological Psychiatry: Cognitive Neuroscience and Neuroimaging. 2018;3:263-73.

ABERRANT TIME-VARYING CROSS-NETWORK INTERACTIONS IN CHILDREN WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER AND THE RELATION TO ATTENTION DEFICITS.

Cai W, Chen T, Szegletes L, et al.

**Background**: Attention-deficit/hyperactivity disorder (ADHD) is thought to stem from aberrancies in large-scale cognitive control networks. However, the exact nature of aberrant brain circuit dynamics involving these control networks is poorly understood. Using a saliency-based triple-network model of cognitive control, we tested the hypothesis that dynamic cross-network interactions among the salience, central executive, and default mode networks are dysregulated in children with ADHD, and we investigated how these dysregulations contribute to inattention.

**Methods**: Using functional magnetic resonance imaging data from 140 children with ADHD and typically developing children from two cohorts (primary cohort = 80 children, replication cohort = 60 children) in a case-control design, we examined both time-averaged and dynamic time-varying cross-network interactions in each cohort separately.

**Results**: Time-averaged measures of salience network centered cross-network interactions were significantly lower in children with ADHD compared with typically developing children and were correlated with severity of inattention symptoms. Children with ADHD displayed more variable dynamic cross-network interaction patterns, including less persistent brain states, significantly shorter mean lifetimes of brain states, and intermittently weaker cross-network interactions. Importantly, dynamic time-varying measures of cross-network interactions were more strongly correlated with inattention symptoms than with time-averaged measures of functional connectivity. Crucially, we replicated these findings in the two independent cohorts of children with ADHD and typically developing children.

**Conclusions**: Aberrancies in time-varying engagement of the salience network with the central executive network and default mode network are a robust and clinically relevant neurobiological signature of childhood ADHD symptoms. The triple-network neurocognitive model provides a novel, replicable, and parsimonious dynamical systems neuroscience framework for characterizing childhood ADHD and inattention

.....

Biol Psychol. 2018;134:30-38.

METHYLPHENIDATE SELECTIVELY MODULATES ONE SUB-COMPONENT OF THE NO-GO P3 IN PEDIATRIC ADHD MEDICATION RESPONDERS.

#### Aasen IE, et al.

Methylphenidate (MPH) has been shown to modulate the amplitude of the no-go P3 component of the event-related potential (ERP; grim, Aasen, & Brunner, 2016). Using group independent component analysis, the no-go P3 from a cued go/no-go task has been separated into two sub-components (Brunner et al., 2013). This study investigated whether sub-components of the no-go P3 could be identified in children with ADHD, and how MPH modulates their amplitudes. ERPs were registered twice (on/off MPH) in 57 children with ADHD classified as medication responders in a four-week medication trial. Two no-go P3 sub-components were identified. In the MPH session, the amplitude of one sub-component, the IC P3no-goearly (mean latency 378 ms, with a central distribution), was significantly larger than at baseline, whereas the other sub-component, the IC P3no-golate (mean latency 428 ms, with a centro-frontal distribution), was not significantly affected. These results add to the literature documenting that the no-go P3 consists of two overlapping phenomena with different functional correlates

.....

Biomedical Research (India). 2017;2017;S455-S460.

EFFECTS OF COMBINATION EXERCISES ON ELECTROENCEPHALOGRAPHY AND FRONTAL LOBE EXECUTIVE FUNCTION MEASURES IN CHILDREN WITH ADHD: A PILOT STUDY.

#### Lee S-K, Song J, Park J-H.

The purpose of the present study was to investigate the effects of exercise on neuropsychological variables of executive function and physiological variables with electroencephalography in children with attention-deficit hyperactivity disorder. The participants included 12 boys in grades 1-4 who were randomly assigned to the combined exercise group (n=6) or control group (n=6). A 60 m exercise program (10-m warm-up, 40 m main exercise, and 10 m cool down) was performed three times a week for a total of 12 weeks. For the electroencephalography, a learning curve was utilized, and the electrodes were firmly attached to the children's scalps. Golden's paediatric stroop color and word test was used to measure executive function in the frontal lobe. After 12 weeks, the F3 and F4 TASK results and color-word scores were significantly increased in the exercise group compared with the control group. The 12 week combination exercise program (jump rope and ball exercises) had positive effects on the electroencephalography and frontal lobe executive function measures of children with attention-deficit hyperactivity disorder

BMC Pediatr. 2018:18.

PREVALENCE OF ATTENTION-DEFICIT/HYPERACTIVITY DISORDER SYMPTOMS AND THEIR ASSOCIATIONS WITH SLEEP SCHEDULES AND SLEEP-RELATED PROBLEMS AMONG PRESCHOOLERS IN MAINLAND CHINA.

Cao H, Yan S, Gu C, et al.

**Background** Attention-deficit/hyperactivity disorder (ADHD) among children is an increasing public health concern. The identification of behavioral risk factors, including sleep quality, has important public health implications for prioritizing behavioral intervention strategies for ADHD. Herein, this study aimed to investigate the prevalence of high levels of ADHD symptoms and to explore the association between sleep schedules, sleep-related problems and ADHD symptoms among preschoolers aged 3 to 6 years in mainland China.

**Methods** A cross-sectional study was conducted, comprising a large sample of 15,291 preschoolers in Ma'anshan city of Anhui Province in China. ADHD symptoms were assessed by the 10-item Chinese version of the Conners Abbreviated Symptom Questionnaire (C-ASQ). Sleep-related variables included caregivers' responses to specific questions addressing children's daytime and nighttime sleep schedules, as well as sleep-related behaviors. Data on other factors were also collected, such as socio-demographic characteristics, TV viewing duration on weekdays and weekends, and outdoor activities. Logistic regression models were used to analyze the relationships between sleep schedules, sleep-related problems and ADHD symptoms.

**Results** Approximately 8.6% of the total sample of preschoolers had high levels of ADHD symptoms, with boys having higher levels than girls (9.9% vs. 7.2%). In the logistic regression analysis, after adjusting for TV viewing duration, outdoor activities, and socio-demographic characteristics, delayed bedtime was significantly associated with a risk of high levels of ADHD symptoms, with odds ratios (OR) of 2.50 [95% confidence interval (CI):  $2.09 \sim 3.00$ ] and 2.04 (95% CI:  $1.72 \sim 2.42$ ) for weekdays and weekends, respectively. Longer time falling asleep ( $\geq 31$  min) (OR = 1.76, 95% CI:  $1.47 \sim 2.11$ ), no naps (OR = 1.57, 95% CI:  $1.34 \sim 1.84$ ) and frequent sleep-related problems (OR = 4.57, 95% CI:  $3.86 \sim 5.41$ ) were also significantly associated with an increased risk of high levels of ADHD symptoms, while longer sleep duration (> 8.5 h) was associated with a decreased risk of high levels of ADHD symptoms (OR = 0.76, 95% CI:  $0.67 \sim 0.87$ ).

**Conclusions** ADHD symptoms are prevalent in preschoolers in Ma'anshan region, China. Undesirable sleep schedules and sleep-related problems among preschoolers confer a risk of ADHD symptoms, highlighting the finding that beneficial and regular sleep habits potentially attenuate ADHD symptoms among preschoolers

.....

Brain Behav. 2018;8.

**DLGAP1** AND **NMDA** RECEPTOR-ASSOCIATED POSTSYNAPTIC DENSITY PROTEIN GENES INFLUENCE EXECUTIVE FUNCTION IN ATTENTION DEFICIT HYPERACTIVITY DISORDER.

Fan Z, Qian Y, Lu Q, et al.

**Objective**: To explore the association of DLGAP1 gene with executive function (EF) in attention deficit hyperactivity disorder (ADHD) children.

**Method**: A total of 763 ADHD children and 140 healthy controls were enrolled. The difference of EF between ADHD and controls was analyzed using the analysis of covariance (ANCOVA), with IQ, sex, and age as covariates. Both the associations of SNPs with EF and three symptom traits of ADHD were conducted using an additive linear regression model by PLINK with the same covariates as ANCOVA.

**Results**: Compared with controls, children with ADHD showed poorer cognitive flexibility and inhibition. Two SNPs (rs2049161, p-value = 5.08e-7, adjusted p-value = 1.63e-4, rs16946051, p-value = 5.18e-7, adjusted p-value = 1.66e-4) survived multiple tests in Trail Making Test. Both SNPs also showed association with TOH (rs2049161, p = 6.82e-4, rs16946051, p = 7.91e-4). Set-based analysis for gene DLGAP1 and its functional pathway DLGAP1-DLG4-NMDA showed they were associated with cognitive flexibility at both gene (p = .0057) and pathway level (p = .0321). Furthermore, the gene and pathway also showed association with ADHD symptom score. The associated SNPs and their LD proxies were related to the expression of DLGAP1 in medulla and frontal cortex.

**Conclusion**: Children with ADHD showed deficit in EF, especially, cognitive flexibility and inhibition. DLGAP1 was associated with cognitive flexibility and plan, and the role of DLGAP1 might be implemented through the complex of DLGAP1-DLG4-NMDA

.....

Brain Imaging Behav. 2017;11:1422-31.

THE EFFECT OF SINGLE-DOSE METHYLPHENIDATE ON RESTING-STATE NETWORK FUNCTIONAL CONNECTIVITY IN ADHD.

#### Silk TJ, Malpas C, Vance A, et al.

We examined the effect of a single dose of methylphenidate (MPH) on whole brain functional connectivity, assessed using resting state functional MRI (rsfMRI), in young people with ADHD. 16 young people with ADHD participated in two rsfMRI scans in a randomized, placebo-controlled study with an acute dose of MPH (20-ámg). 15 typically developing controls also performed the task under placebo conditions. The network-based statistic (NBS) was used to identify differential connectivity patterns between the MPH and placebo conditions in the ADHD group. Mean connectivity of the resulting sub-network was examined in the ADHD and control groups. Resting state functional connectivity (RSFC) analysis revealed significantly reduced connectivity under MPH compared to placebo in young people with ADHD. Findings were robust across a range of thresholds. No sub-networks of increased connectivity were found at any threshold. Mean connectivity of the identified sub-network was significantly higher in ADHD individuals in the placebo condition compared to controls, however there was no difference between MPH condition and controls. We demonstrated a significant MPH-related reduction in RSFC in a large, robust network primarily involving occipital, temporal and cerebellar regions, and visual, executive and default mode networks. These findings suggest that MPH is ΓÇÿnormalisingΓÇÖ a higher RSFC in young people with ADHD. This study is a novel addition to the understanding of treatment effects on the brain in ADHD

.....

Cephalalgia. 2017;37:180.

BURDEN OF HEADACHE DISORDERS AT ATTENTION DEFICIT HYPERACTIVITY DIAGNOSED CHILDREN AND THEIR PARENTS.

#### Kucuk MO, G++ler G, Tufan E, et al.

**Objectives**: Attention deficit and hyperactivity disorder (ADHD) is common among children and adolescents with a worldwide prevalence of 5.3% and is considered to be an important factor leading to poor academic performance and poor quality of life. Headache is one of the most common chronic disorder with a prevalence of 10-20% in the school-age population and often accompanied by severe impairments, including low quality of life, low emotional functioning, school absenteeism, and poor academic performance. The prevalence of ADHD among children with headache are still contradictory and the prevalence of headache disorders in ADHD is not well studied. The clinical study aimed to evaluate burden of primary headache among ADHD children and parents and results compared age and sex matched healthy controls.

**Methods**: The study comprised children and adolescents aged 6-18 years with ADHD according to DSM-5, healthy controls and parents of these 2 groups were referred by the child and adolescent psychiatrist for neurological assessment to the neurologist at Mersin University Medical Faculty during drug navy period for patients. Both the interview and the questionnaire included questions regarding demographics, patient' and families' medical history, headaches characteristics, and other medical history obtained by experienced nerulogists and psychiatrists. Headache diagnosis based to ICHD-3 beta criteria.

**Results**: The study group comprised of 117 ADHD children and 111 age and sex matched healthy controls. Median of age was 11 years (6-18) in ADHD group and 12 (8-16) years for healthy controls. Headache was common for both groups and was significantly more common in ADHD patients (59,0% & 37,8%) (p=0,002). While episodic and chronic migraine found significantly common in ADHD children, frequent episodic TTH was common in control group. The most frequent diagnosis was episodic migraine for ADHD and episodic TTH for control group. The overall prevalence of migraine for ADHD group estimated 26,5%, and 9,9% for healthy controls. We analyzed characteristics of mothers of ADHD (ADHD-M) and healthy controls mothers

(HC-M) headache. Primary headache disorders was significantly more common for ADHD-M (90,5% & 65,6%). While migraine, particularly chronic migraine was more common in ADHD-M, episodic tension type headache was more common at health controls mothers (HC-M). The overall prevalence of migraine for ADHD-Ms was 72% and estimated 42,9% for HC-Ms. The analyses of the fathers of study group performed. The prevalence of headache was similar at two groups. The most common headache disorder was infrequent TTH at ADHD fathers and frequent TTH at control groups' fathers. The overall prevalence of migraine for ADHD fathers estimated 21% and was %13,7 for healthy controls fathers. Chronic migraine was significantly more common at ADHD fathers.

**Conclusion**: We observed headache is more prevalent in ADHD children than controls and also ADHD-mothers have more common headache. Migraine and chronic migraine is more prevalent in them, while tension type headache was more common in mothers of healthy controls. Knowledge of common biologic systems involved would not only help physicians provide better care for their patients but may also provide some clues regarding sources of heterogeneity of ADHD

.....

Child Fam Behav Ther. 2018 Jan;40:65-83.

PARENT-CHILD INTERACTION THERAPY AND ADHD: A CASE STUDY WITH A HEARING CHILD OF A DEAF FATHER AND A HEARING MOTHER.

#### Tan SY, Steding LH, Coates EE, et al.

Parent-Child Interaction Therapy (PCIT) has demonstrated promising evidence in its implementation with deaf and hard-of-hearing (DHH) families. This case study presents the implementation of PCIT with a hearing mother, a deaf father, and their 7-year-old hearing son with Attention-Deficit/Hyperactivity Disorder (ADHD) and oppositional behaviors, using the assistance of certified interpreters. Results documented improvement in child behavior, parenting skills and stress, and parent-child communication. Notably, paternal ratings showed greater improvement across these outcomes than maternal ratings. Overall, PCIT continues to demonstrate its effectiveness as a treatment option for DHH families with children with challenging behaviors. The limitations and implications are discussed

.....

Child Adolesc Psychiatr Clin N Am. 2017 Jul;26:597-609.

PARTNERSHIPS WITH PRIMARY CARE FOR THE TREATMENT OF PRESCHOOLERS.

#### Marcus SM, Malas NM, Quigley JM, et al.

This article reviews mental health access issues relevant to preschool children and data on this population obtained through the Michigan Child Collaborative Care Program (MC3). The MC3 program provides telephonic consultation to primary care physicians (PCPs) in 40 counties in Michigan and video telepsychiatric consultation to patients and families. Attention-deficit/hyperactivity disorder and disruptive behavioral disorders are frequent initial presenting diagnoses, but autism spectrum disorders, parent-child relational issues, trauma, and posttraumatic stress disorder should also be considered. Collaborative care programs provide promising ways to promote access to child psychiatric services when these services are distant to local PCP offices

.....

Child Care Health Dev. 2017 Jul:43:489-98.

EDUCATORS' EXPERIENCES OF MANAGING STUDENTS WITH ADHD: A QUALITATIVE STUDY.

Moore DA, Russell AE, Arnell S, et al.

**BACKGROUND**: The symptoms of attention-deficit/hyperactivity disorder are associated with difficulty coping with the social, behavioural and academic components of school. Compared with medication and other non-pharmacological treatment, there is less evidence relating to school-based interventions to support children with ADHD. There is additionally an absence of any research focused on the experiences and

practices of educators in the UK around how they work with children who are inattentive, impulsive and hyperactive.

**MÉTHODS**: Forty-two educational practitioners from primary, secondary and alternate provision schools in the UK participated in focus groups or individual interviews that explored (1) their experiences of managing students with ADHD in the classroom and (2) factors that helped and hindered them in this endeavour. Transcripts were analysed using thematic analysis.

**RESULTS**: Analysis identified six themes: broad strategies, student-centred, inclusive strategies, labelling, medication and relationships. Participants' experiences of managing students with ADHD drew upon a wide range of strategies that typically involved responding to individual needs in an inclusive manner, so individuals with ADHD could access the classroom with their peers. Participants spoke about three factors that helped and hindered managing students with ADHD. Labelling of students with ADHD was reported, with the negative aspects of labelling, such as stigmatization, affecting the classroom. Educators reported mixed experiences regarding the helpfulness of medication; where helpful, it allowed the use of strategies in the classroom. Although students with ADHD were described as having rollercoaster relationships, positive relationships were considered key to the support of children with these difficulties.

**CONCLUSIONS**: This study suggests that factors such as attitudes towards ADHD, relationships experienced by students with ADHD and other treatments being delivered need to be carefully considered before strategies are put in place in the classroom. This study supports the need for further work on the implementation of evidence-based school interventions for ADHD

.....

Child Neuropsychol. 2018;1-21.

# A CRITICAL APPRAISAL OF THE ROLE OF NEUROPSYCHOLOGICAL DEFICITS IN PRESCHOOL ADHD. Sjöwall D. Thorell LB.

The present study aimed at improving our understanding of the role of neuropsychological deficits in preschool Attention Deficit Hyperactivity Disorder (ADHD). The study included 52 children in the ADHD group and 72 controls (age 4ΓCô6-ávears). Both laboratory measures and teacher reports of executive deficits (i.e., working memory, inhibition, and shifting), delay-related behaviors (i.e., the preference for minimizing delay), and emotional functions (i.e., emotion recognition and regulation) were included. Variable-oriented analyses were complemented with person-oriented analyses (i.e., identifying the proportion of patients considered impaired). Results showed that the ADHD group differed from controls with regard to all measures of executive functioning and most measures of delay-related behaviors, but few differences were found for emotional functioning. A substantial subgroup (23%) of children with ADHD did not have a neuropsychological deficit in any domain. There were subgroups with executive or delay-related deficits only, but no pure emotional subgroup. The overlap between different neuropsychological deficits was much larger when teacher reports were used as opposed to laboratory measures. Regarding functional impairments, large mean differences were found between the ADHD group and controls. However, neuropsychological deficits were not able to explain individual variations in daily life functioning among children with ADHD. In conclusion, the present study identified some important methodological and theoretical issues regarding the role of neuropsychological functioning in preschool ADHD

Child Neuropsychol. 2018;1-8.

WAITING IMPULSIVITY: A DISTINCTIVE FEATURE OF ADHD NEUROPSYCHOLOGY?

Van DJ, Morsink S, Van der Oord S, et al.

Impulsivity is a core feature of attention-deficit hyperactivity disorder (ADHD). It has been conceptualized in a number of different ways. In the current article, we examine how the new concept of  $\Gamma \subseteq \mathbb{C}$  waiting impulsivity  $\Gamma \subseteq \mathbb{C}$ , which refers to premature responding before a scheduled target appears, adds to our understanding of impulsivity in ADHD. Sixty children (8 $\Gamma \subseteq \mathbb{C}$ 012-áyears old; 30 ADHD; 30 typically developing controls) completed the 4-choice serial reaction time task, a measure of waiting impulsivity, alongside tasks measuring inhibitory control and temporal discounting and questionnaires measuring behavioral disorder

Newsletter – ADHD marzo 2018

symptoms, delay aversion, and various aspects of impulsivity. A multiple logistic regression model was used to explore the contribution of the primary task outcomes to predict group membership. Children with ADHD displayed more waiting impulsivity and less inhibitory control; they did not differ in temporal discounting. There was no correlation between waiting impulsivity and inhibitory control. Waiting impulsivity was correlated with parent-reported ratings of hyperactivity/impulsivity, inattention, oppositional defiant disorder (ODD), and conduct disorder (CD) and with self-reported delay aversion ratings. Only waiting impulsivity was a significant predictor of ADHD status. In conclusion, waiting impulsivity is distinct from inhibitory control deficits and predicts ADHD status independently of it. Future research needs to examine the relationship with delay aversion and ODD/CD more thoroughly

.....

Child Psychiatry Hum Dev. 2018 Feb;49:42-52.

MATERNAL RESPONSIVENESS AS A PREDICTOR OF SELF-REGULATION DEVELOPMENT AND ATTENTION-DEFICIT/HYPERACTIVITY SYMPTOMS ACROSS PRESCHOOL AGES.

#### Pauli-Pott U, Schloß S, Becker K.

Preschool-age 'hot' executive function capacity (i.e. reward-related effortful control) represents an early kind of self-regulation that is involved in social adjustment development as well as the development of subtypes of attention-deficit/hyperactivity disorder (ADHD). Early self-regulation development might be malleable by responsive parenting. We analyzed whether maternal responsiveness/sensitivity predicts reward-related control (RRC) development within the preschool period, and whether RRC mediates a negative link between maternal responsiveness and ADHD symptoms. A sample of 125 preschoolers and their families were seen at the ages of 4 and 5 years. Maternal responsiveness/sensitivity was assessed via home observations, RRC by neuropsychological tasks, and ADHD symptoms by a structured clinical parent interview. Maternal responsiveness/sensitivity predicted RRC development. The negative link between maternal responsiveness/sensitivity at 4 years and ADHD symptoms at 5 years was mediated by RRC performance at 5 years. Preschoolers showing ADHD symptoms combined with low RRC capacity in particular might benefit from responsive/sensitive parenting

.....

Child Psychiatry Hum Dev. 2018 Feb;49:155-62.

PARENT PERCEPTIONS OF MEDICATION TREATMENT FOR PRESCHOOL CHILDREN WITH ADHD.

#### Hart KC, Ros R, Gonzalez V, et al.

This study sought to examine parent perceptions of medication use for 151 preschool children (Mage = 5.05 years, 78% male, 82% Hispanic/Latino) with or at-risk for ADHD who were medication naive. Parents completed questionnaires regarding family background and perceptions of medication treatment. Parents and teachers completed ratings of child diagnostic symptomatology, behavioral functioning, and functional impairment. Results indicate that only 45% of parents were open to the possibility of medication. No associations were found between child demographics, severity of ADHD symptoms, or level of functional impairment and parental openness to medication. On the other hand, children of parents who were open to medication tended to have higher levels of oppositionality and aggression (as reported by parents but not teachers) compared with children of parents who were not open to medication. These findings are discussed in the context of early intervention given their implications for a variety of treatment providers

Chin Med J. 2018:131:648-56.

NEUROPSYCHOLOGICAL PROFILE RELATED WITH EXECUTIVE FUNCTION OF CHINESE PRESCHOOLERS WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER: NEUROPSYCHOLOGICAL MEASURES AND BEHAVIOR RATING SCALE OF EXECUTIVE FUNCTION-PRESCHOOL VERSION.

# Zhang H-F, Shuai L, Zhang J-S, et al.

**Background**: Previous studies have found that schoolchildren with attention-deficit/hyperactivity disorder (ADHD) showed difficulties in neuropsychological function. This study aimed to assess neuropsychological function in Chinese preschoolers with ADHD using broad neuropsychological measures and rating scales and to test whether the pattern and severity of neuropsychological weakness differed among ADHD presentations in preschool children.

**Methods**: The 226 preschoolers (163 with ADHD and 63 controls) with the age of 4-5 years were included and assessed using the Behavior Rating Scale of Executive Function-Preschool Version (BRIEF-P) and a series of tests to investigate neuropsychological function.

Results: Preschoolers with ADHD showed higher scores in all domains of the BRIEF-P (inhibition: 30.64 ±  $5.78 \text{ vs.} + 20.69 \pm 3.86$ , P < 0.001; shift:  $13.40 \pm 3.03 \text{ vs.} + 12.41 \pm 2.79$ , P = 0.039; emotional control:  $15.10 \pm 1.00 \pm 1.00$  $3.53 \text{ vs.} 12.20 \pm 2.46$ , P < 0.001; working memory:  $28.41 \pm 4.99 \text{ vs.} 20.95 \pm 4.60$ , P < 0.001; plan/organize:  $17.04 \pm 3.30 \text{ vs.} 13.29 \pm 2.40, P < 0.001)$  and lower scores of Statue (23.18 ± 7.84 vs.28.27 ± 3.18, P = 0.001), Word Generation (15.22  $\pm$  6.52 vs.19.53  $\pm$  7.69, P = 0.025), Comprehension of Instructions (14.00  $\pm$  $4.44 \text{ vs.} 17.02 \pm 3.39$ , P = 0.016), Visuomotor Precision (P < 0.050), Toy delay (P = 0.048), and Matrices tasks (P = 0.011), compared with normal control. In terms of the differences among ADHD subtypes, all ADHD presentations had higher scores in several domains of the BRIEF-P (P < 0.001), and the ADHDcombined symptoms (ADHD-C) group had the poorest ratings on inhibition and the ability to Plan/Organize. For neuropsychological measures, the results suggested that the ADHD-C group had poorer performances than the ADHD-predominantly inattentive symptoms (ADHD-I) group on Statue tasks (F = 7.34,  $n^2 = 0.12$ , P < 0.001). Furthermore, the ADHD-hyperactive/impulsive symptoms group had significantly poorer performances compared to the ADHD-C group in the Block Construction task (F = 4.89, η2 = 0.067, P = 0.003). However, no significant group differences were found between the ADHD-I group and normal control. Conclusion: Based on the combined evaluation of performance-based neuropsychological tests and the BRIEF-P, preschoolers with ADHD show difficulties of neuropsychological function in many aspects

Chronic Illness. 2018;14:69-75.

PARENTAL HAPPINESS AND STRAIN AMONG YOUNG ADULT PARENTS DIAGNOSED WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER.

# Kroeger RA.

This study used data from the National Longitudinal Study of Adolescent to Adult Health (Add Health) to examine whether young adult parents diagnosed with Attention Deficit Hyperactivity Disorder experience less parental happiness and/or more parental strain than their counterparts not diagnosed with Attention Deficit Hyperactivity Disorder. Results from logistic regression models indicated that young adult parents ever diagnosed with Attention Deficit Hyperactivity Disorder have significantly greater odds of feeling overwhelmed as parents and significantly lower odds of feeling close to their children or happy in their role as parents compared to those never diagnosed with Attention Deficit Hyperactivity Disorder. Potential implications of these results for scholars as well as health professionals treating adult Attention Deficit Hyperactivity Disorder patients with children are discussed

Newsletter – ADHD marzo 2018

Chronobiol Int. 2016;33:1433-43.

SLEEP QUALITY, CHRONOTYPE AND SOCIAL JETLAG DIFFERENTIALLY ASSOCIATE WITH SYMPTOMS OF ATTENTION DEFICIT HYPERACTIVITY DISORDER IN ADULTS.

#### McGowan NM, Voinescu BI, Coogan AN.

Attention deficit hyperactivity disorder (ADHD) is a common neurobehavioural disorder which has been associated with sleep and circadian rhythm disturbances. Numerous studies have linked evening circadian typology with traits and behaviours associated with the disorder, although a precise reason for this relationship has not been clarified. The current study examines ADHD symptoms, impulsivity, cognitive failures, sleep quality and chronotype in a cohort of healthy young adults (N = 396). Results show significant, small magnitude associations between mid-point of sleep on free days, social jetlag (SJL) and ADHD symptoms and impulsivity, although not with cognitive failures. Similarly, sleep quality is also associated with ADHD symptoms and impulsivity. Group-wise approaches show that higher SJL is associated with significantly more ADHD symptoms and impulsivity, and later mid-sleep on free days is also associated with more ADHD symptoms. Stepwise multiple linear regression reveals that, when controlling for age and sex, SJL but not mid-sleep on free days is a significant predictor of ADHD symptoms and impulsivity. These results indicate that SJL may be an important factor to consider when exploring circadian rhythm associations with ADHD symptoms

.....

Clin EEG Neurosci, 2017 Jul:48:243-45.

THE UTILITY OF EEG IN ATTENTION DEFICIT HYPERACTIVITY DISORDER: A REPLICATION STUDY.

#### Swatzyna RJ, Tarnow JD, Roark A, et al.

The routine use of stimulants in pediatrics has increased dramatically over the past 3 decades and the long-term consequences have yet to be fully studied. Since 1978 there have been 7 articles identifying electroencephalogram (EEG) abnormalities, particularly epileptiform discharges in children with attention deficit hyperactivity disorder (ADHD). Many have studied the prevalence of these discharges in this population with varying results. An article published in 2011 suggests that EEG technology should be considered prior to prescribing stimulants to children diagnosed with ADHD due to a high prevalence of epileptiform discharges. The 2011 study found a higher prevalence (26%) of epileptiform discharges when using 23-hour and sleep-deprived EEGs in comparison with other methods of activation (hyperventilation or photostimulation) and conventional EEG. We sought to replicate the 2011 results using conventional EEG with the added qEEG technologies of automatic spike detection and low-resolution electromagnetic tomography analysis (LORETA) brain mapping. Our results showed 32% prevalence of epileptiform discharges, which suggests that an EEG should be considered prior to prescribing stimulant medications

.....

Combination therapy was significantly more frequent in the adult group (p=0.015).

Clinical Neuropsychopharmacology and Therapeutics. 2017;8:1-6.

CIRCUMSTANCES OF PRESCRIPTIONS FOR ADHD TREATMENT AND CONCURRENT MEDICATION IN JUVENILES AND ADULTS AT A PSYCHIATRIC INSTITUTION IN JAPAN.

### Fukunaga R, Yasugawa S, Abe Y, et al.

**Purpose**: Relatively few ADHD drugs are available in Japan, but psychotropics are often used for the comorbidity of ADHD. We aimed to compare juvenile and adult patients in terms of drugs used for ADHD. **Methods**: We retrospectively surveyed the circumstances of prescriptions for atomoxetine and concurrent medications for ADHD patients (36 men, 39 women) using electronic medical records from a single-department psychiatric hospital in rural Japan. Mean dosage, period and rate of administration continuation, side effects, reasons for cessation, comorbid diagnoses, and use of concurrent medication were statistically compared between juvenile (<18 years old) and adult (18 years old) groups using the t-test and 2 test. **Results**: Continuation rate was significantly higher in the adult group (43.5%) than in the juvenile group (20.7%; p= 0.043). In the juvenile group, 65.5% received monotherapy and 34.5% received combination therapy, compared to monotherapy for 37.0% and combination therapy for 63.0% in the adult group.

**Discussion**: These findings were attributed to differences in motivations for medical treatment and carereceiving patterns between groups. Since juvenile people often start treatment for ADHD as a primary condition, rather than as a comorbidity, concomitant medications are less frequent. Juvenile patients tend to drop out because of poor subjective symptoms. Among adults, treatment for ADHD often begins as treatment of comorbidity, so concomitant medications and maintenance therapy are more frequent than among juvenile patients

.....

Clin Pediatr. 2017.

NEURODEVELOPMENTAL DISORDERS IN THE PICU POPULATION.

#### Sobotka SA, Peters S, Pinto NP.

Attention deficit hyperactivity disorder (ADHD), affecting 11% of children and adolescents, increases risk for injury and may predispose children to illness. However, the prevalence of ADHD and other developmental disorders in the pediatric intensive care unit (PICU) has not been previously studied. We performed a single-center, prospective cohort study of children aged 6 to 12 years who were hospitalized in the PICU from May through August 2016. Parents described their child \$\Gamma\text{Q}\text{Os}\$ educational and neurodevelopmental history, and completed ADHD and emotional/behavioral disorder screening on enrollment and 1 month after discharge. Twenty-four children were enrolled. Ten patients (42%) had a prior neurodevelopmental diagnosis, and 7 (29%) met study criteria for ADHD. Children hospitalized for critical illness have a high prevalence of neurodevelopmental disabilities and are more susceptible to the impact of critical illness on development and behavior. More research is needed to better understand how to support this vulnerable population after critical illness

.....

Clin Pediatr. 2018.

HAVING A REGULAR PRIMARY CARE PROVIDER IS ASSOCIATED WITH IMPROVED MARKERS OF WELL-BEING AMONG CHILDREN WITH ATTENTION-DEFICIT HYPERACTIVITY DISORDER.

# Rubinstein M, Ruest S, Amanullah S, et al.

We examined the association between having a regular primary care physician (PCP) and measures of flourishing and academic success in children with attention-deficit hyperactivity disorder (ADHD). We performed a cross-sectional study using data from the 2011-2012 National Survey of Children's Health. Children aged 6 to 17 years with a diagnosis of ADHD were included in the study (n = 8173). The exposure was whether the guardian identified a regular PCP for their child. The outcomes were parental-reported measures of child well-being and academic performance. Among the study population, 8.9% reported no regular PCP. These children were found to be significantly less likely to finish assigned tasks (adjusted odds ratio [OR] = 0.52, 95% confidence interval [CI] = 0.35-0.79), care about school (adjusted OR = 0.62, 95% CI = 0.38-0.92), and finish homework (adjusted OR = 0.58, 95% CI = 0.36-0.88). There were no differences in other examined outcomes. Enhancing longitudinal care for this population may optimize their academic performance

.....

CNS Drugs. 2018;1-10.

PERINATAL OUTCOMES OF WOMEN DIAGNOSED WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER: AN AUSTRALIAN POPULATION-BASED COHORT STUDY.

Poulton AS, Armstrong B, Nanan RK.

**Background**: Attention-deficit/hyperactivity disorder (ADHD) is common and may require treatment in adulthood. We aimed to investigate the treatment patterns and perinatal outcomes of women with any history of stimulant treatment for ADHD.

**Methods**: We used health records of the New South Wales (NSW, Australia) population to compare perinatal outcomes of women treated with stimulants (dexamphetamine or methylphenidate) for ADHD from 1982 to

2012 who gave birth between 1994 and 2012, with perinatal outcomes of women with no known ADHD or stimulant treatment (comparison cohort). Five comparison women, matched by maternal age and infant year of birth, were selected for each treated woman. Pregnancy outcome odds ratios in the two groups were adjusted for confounders including maternal age and smoking.

Results: Of 5056 women treated for ADHD with stimulant medication, 3351 (66.3%) had stimulant treatment documented before the index pregnancy but not within 1 year before the expected date of delivery, 175 (3.5%) had stimulant treatment before and possibly during pregnancy (stimulant prescription within the 12 months directly before the expected date of the index birth and earlier), and 1530 (30.2%) had no stimulant treatment until after the index pregnancy. Treatment for ADHD at any time (before, before and during and only after the index pregnancy) was associated with reduced likelihood of spontaneous labour odds ratios (ORs) 0.7 [0.7, 0.8], 0.7 [0.5, 0.9], and 0.7 [0.7, 0.8], respectively and increased risk of caesarean delivery (1.2 [1.1, 1.3], 1.3 [0.9, 1.8], 1.3 [1.1, 1.4]); active neonatal resuscitation (1.2 [1.0, 1.3], 1.7 [1.1, 2.7], 1.3 [1.0, 1.7]); and neonatal admission > 4 h (1.2 [1.1, 1.3], 1.7 [1.2, 2.4], 1.2 [1.0, 1.4]). Treatment before or before and during pregnancy was, in addition, associated with increased risk of pre-eclampsia (1.2 [1.0, 1.4], 1.5 [0.8, 2.6]); preterm birth < 37 weeks (1.2 [1.0, 1.3], 1.4 [0.9, 2.3]); and 1-min Apgar < 7 (1.2 [1.1, 1.3], 2.0 [1.4, 2.9]). Stimulant prescribing was low during pregnancy (3.5% of women received such a prescription) and dropped during the 12 months before the due date from an average of 24.7 prescriptions per month in the first 6 months to 4.5 per month in the final 6 months.

**Conclusions**: Compared with no treatment, ADHD stimulant treatment at any time was associated with small increases in the risk of some adverse pregnancy outcomes; treatment before, or before and during pregnancy, was associated with additional adverse outcomes, even after a treatment-free period of several years. None of these associations can be confidently attributed to stimulant treatment; in all cases ADHD per se or correlates of it could be responsible for the association

.....

Contemporary School Psychology. 2018 Mar;22:1-17.

HISTORICAL OVERVIEW OF ATTENTION DEFICIT-HYPERACTIVITY DISORDER AND NEUROFEEDBACK: IMPLICATIONS FOR ACADEMIC ACHIEVEMENT, ASSESSMENT, AND INTERVENTION IN SCHOOLS.

#### La Marca JP.

From the first mention of impairments in attention in the scientific literature by the Scottish physician Alexander Crichton in 1798, the correlation between educational attainment and learning has been persistently noted. Since then, the impact of attention deficits on school achievement has been a central component in a significant portion of research, despite continual disagreements within the scientific community on identification, diagnosis, and efficacious interventions to address core symptoms of what is now referred to as Attention Deficit-Hyperactivity Disorder (ADHD). This article provides the historical context in which the construct of ADHD was developed, as well as a discussion of two commonly used interventions to address symptoms of ADHD (e.g., pharmaceuticals and the use of electroencephalographic [EEG] operant conditioning, or 'neurofeedback.'). While use of pharmaceutical interventions is relegated only to medical professionals, neurofeedback may have the potential to be used by highly trained special educators and school psychologists in academic settings

.....

Drug Alcohol Depend. 2018;184:48-56.

EARLY ONSET TOBACCO CIGARETTE SMOKERS EXHIBIT DEFICITS IN RESPONSE INHIBITION AND SUSTAINED ATTENTION.

Mashhoon Y, Betts J, Farmer SL, et al.

**Background**: Initiation of cigarette smoking during adolescence coincides with structural and cognitive neuromaturation. Thus, early onset smokers (EOS; initiated <16 years old) may be at unique risk of altered development of executive function relative to late onset smokers (LOS; initiated >16 years old). This study quantified the effects of age of smoking onset on response impulsivity and inhibitory control using a novel smoking Go/NoGo task (Luijten et al., 2011).

**Methods**: Nicotine deprived adult EOS (n = 10) and LOS (n = 10) and adult healthy non-smokers (HNS; n = 10) were shown smoking-related and neutral images with either a blue (Go) or yellow (NoGo) frame. Participants were instructed to respond to blue-framed Go trials quickly and accurately, and withhold responding for yellow-framed NoGo trials.

**Results**: EOS made more Go response accuracy errors (p 0.02) and failed more frequently to inhibit responses to NoGo trials (p < 0.02) than LOS and HNS. EOS also made more errors in inhibiting responses to smoking-related (p 0.02) and neutral (p  $\Gamma$ eñ 0.02) NoGo trials. EOS reported greater baseline craving for cigarette smoking than LOS (p < 0.04), and craving was significantly associated with greater omission errors (p 0.04).

**Conclusions**: EOS exhibited greater difficulty than LOS in responding accurately to Go stimuli and withholding responses to both smoking and neutral NoGo stimuli, indicating greater response impulsivity, poor attention, and deficits in response inhibition. These findings suggest that EO smoking, in particular, contributes to diminished task-related attention and inhibitory control behaviors in adulthood and provide support for the tobacco-induced neurotoxicity of adolescent cognitive development (TINACD) theory (DeBry and Tiffany, 2008)

.....

Drug Alcohol Depend. 2018;186:154-58.

DOES EXPOSURE TO PARENTAL SUBSTANCE USE DISORDERS INCREASE OFFSPRING RISK FOR A SUBSTANCE USE DISORDER? A LONGITUDINAL FOLLOW-UP STUDY INTO YOUNG ADULTHOOD.

Yule AM, Wilens TE, Martelon M, et al.

**Objective**: The main aim of this study was to examine the risk of exposure to parental substance use disorders (SUD; alcohol or drug abuse or dependence) on the risk for SUD in offspring with and without attention deficit hyperactivity disorder (ADHD) followed into young adult years.

**Methods**: Subjects were derived from two longitudinal case-control studies of probands of both sexes, 6-17 years, with and without DSM-III-R ADHD and their parents. Probands were followed for ten years into young adulthood. Probands with a parental history of non-nicotine SUD were included in this analysis. Exposure to SUD was determined by active non-nicotine parental SUD while the parent was living with their child after birth. Cox proportional hazard models were used to calculate the risk of non-nicotine SUD in offspring.

**Results**: 171 of the 404 probands reassessed at ten-year follow up had a family history of parental SUD. 102 probands were exposed to active parental SUD. The average age of our sample was  $22.2 \pm 3.5$  years old. Exposure to maternal but not paternal SUD increased offspring risk for an alcohol use disorder in young adulthood independently of ADHD status (OR: 2.7; 95% CI: 1.1, 6.9; p = 0.04).

**Conclusion**: Exposure to maternal SUD increases the risk for an alcohol use disorder in offspring ten years later in young adult years irrespective of ADHD status

Duzce Med J. 2016:18:91-94.

INVESTIGATION OF CLINICAL AND SOCIODEMOGRAFIC VARIABLES ASSOCIATED WITH ATTENTION DEFICIT AND HYPERACTIVITY SYMPTOMS IN UNIVERSITY STUDENTS.

Yeil R et al

**Objective**: The aim of this study was to investigate sociodemographic and clinical variables that might be associated with ADHD in adults trained in music and science departments.

**Material and Method**: The study was conducted at In University between January and June 2014. 52 students from music and 52 students from science teacher department between the ages of 18-25 without psychiatric and neurological disease were included in the study. The students were matched in terms of age, sex, duration of education and hand preference. The Turgay Adult Attention Deficit and Hyperactivity Disorder (ADHD) Self-Report Scale was administered to the students.

**Results**: The mean age of 44 male and 58 male participants was  $20.39 \pm 1.99$ . There were no significant differences between the areas of music and science in terms of class level, family history of mental illness, childhood trauma exposure, experience of addictive substance. Department type, class level and family

history of mental illness did not significantly affect ADHD scale scores. Hyperactivity (p=0.02) and problems (p=0.001) subscale and total scores (p=0.001) of students with childhood physical trauma exposure were significantly higher than those without exposure. The students with experience using substance were significantly higher problem subscale scores than those without experience (p=0.04).

**Conclusion**: Childhood physical trauma and substance use experience were found to be associated with ADHD symptoms, but there was no difference between music and science domains in terms of ADHD. Knowing the factors associated with ADHD in adulthood will help to treat this disorder by increasing awareness

.....

Early Hum Dev. 2017 Jul;110:44-49.

LONG-TERM ATTENTION DEFICITS COMBINED WITH SUBCORTICAL AND CORTICAL STRUCTURAL CENTRAL NERVOUS SYSTEM ALTERATIONS IN YOUNG ADULTS BORN SMALL FOR GESTATIONAL AGE.

Suffren S, Angulo D, Ding Y, et al.

**BACKGROUND**: Being born small for gestational age has been associated with neurodevelopmental disabilities and smaller gray matter volumes in childhood. However, it is not known if these changes persist in adults and whether SGA has any impact on attention memory and IQ.

**AIMS**: The goal of this study was to evaluate the association between birth weight and gray matter anatomy in adults born small for gestational age at term, in relation to IQ, attention and memory.

**MATERIALS AND METHODS**: This prospective follow-up study at age 20 included 39 adults born small for gestational age at term and 37 adults born appropriate for gestational age at term. Detailed neurocognitive skills were assessed (IQ, attention and memory). Anatomical images were analyzed using Voxel-Based-Morphometry and FreeSurfer.

**RESULTS**: Adults born small for gestational age at term had lower performances in subtests assessing attention and executive functions. They also showed smaller total intracranial volume; smaller volumes and surface areas in the frontal lobe, inferior/middle parietal and temporal gyrus; smaller cerebellum, thalamus and basal ganglia volumes. Interestingly, all these structures correlated with attention subtests.

**CONCLUSION**: These results highlight the persistent effects of being born small for gestational age on attention and associated brain structures

.....

Encephale. 2017 May:43:268-72.

"ATTENTION DEFICIT HYPERACTIVITY DISORDER IN FORENSIC PSYCHIATRY: A REVIEW".

# Galland D, Tisserant I, Notardonato L.

**INTRODUCTION**: Attention deficit hyperactivity disorder (ADHD) is one of the most common and challenging childhood neurobehavioral disorders. ADHD may have behavioral consequences and involvements in minor and serious crimes. Our work aims to establish links between ADHD and forensic psychiatry.

**METHODS**: A review of international scientific literature concerning the relationship between ADHD and forensic psychiatry was conducted using the PudMed electronic database. We used the Mesh terms: "attention deficit hyperactivity disorder" and "forensic psychiatry". We also used the "related articles" function of PubMed, the bibliography of selected articles and the Google Scholar database to identify possible additional papers.

**RESULTS**: The prevalence of ADHD in prison populations may vary but remain higher than those found in the general population. Violence committed by a person with ADHD seems to be against other persons rather than property offences. Reactive-impulsive violence seems to be more prevalent than pro-active instrumental violence. The existence of ADHD does not appear as a risk factor of recidivism. The violence risk may be increased by the occurrence of comorbidities as conduct disorders and mental deficiency. There may exist a preferential association between ADHD and antisocial personality disorder or substance abuse which both increase the risk of violence.

**DISCUSSION**: To put in perspective forensic psychiatry and ADHD allowed us to identify typology of violence, epidemiological aspect of ADHD in a prison environment and comorbidities involved in the risk of

violence. This research permits to precise elements of prevention, diagnosis and assistance in the management of violent behaviour in ADHD and in expert practice

.....

Encephale. 2018.

FACIAL EMOTION RECOGNITION IN CHILDREN WITH OR WITHOUT ATTENTION DEFICIT/HYPERACTIVITY DISORDER: IMPACT OF COMORBIDITY.

Maire J, Galera C, Roux S, et al.

**OBJECTIVES**: This study sought to assess facial emotion recognition deficit in children with Attention Deficit/Hyperactivity Disorder (ADHD) and to test the hypothesis that it is increased by comorbid features.

**METHOD**: Forty children diagnosed with ADHD were compared with 40 typically developing children, all aged from 7 to 11years old, on a computerized facial emotion recognition task (based on the Pictures of Facial Affect). Data from parents' ratings of ADHD and comorbid symptoms (on the Conners' Revised Parent Rating Scale) were also collected.

**RESULTS**: Children with ADHD had significantly fewer correct answer scores than typically developing controls on the emotional task while they performed similarly on the control task. Recognition of sadness was especially impaired in children with ADHD. While ADHD symptoms were slightly related to facial emotion recognition deficit, oppositional symptoms were related to a decrease in the number of correct answers on sadness and surprise recognition.

**CONCLUSION**: Facial emotion recognition deficit in children with ADHD might be related to an impaired emotional process during childhood. Moreover, Oppositional Defiant Disorder seems to be a risk factor for difficulties in emotion recognition especially in children with ADHD

.....

Environ Res. 2018;164:149-57.

ADVERSE PHYSIOLOGICAL AND PSYCHOLOGICAL EFFECTS OF SCREEN TIME ON CHILDREN AND ADOLESCENTS: LITERATURE REVIEW AND CASE STUDY.

#### Lissak G

A growing body of literature is associating excessive and addictive use of digital media with physical, psychological, social and neurological adverse consequences. Research is focusing more on mobile devices use, and studies suggest that duration, content, after-dark-use, media type and the number of devices are key components determining screen time effects. Physical health effects: excessive screen time is associated with poor sleep and risk factors for cardiovascular diseases such as high blood pressure, obesity, low HDL cholesterol, poor stress regulation (high sympathetic arousal and cortisol dysregulation), and Insulin Resistance. Other physical health consequences include impaired vision and reduced bone density. Psychological effects: internalizing and externalizing behavior is related to poor sleep. Depressive symptoms and suicidal are associated to screen time induced poor sleep, digital device night use, and mobile phone dependency. ADHD-related behavior was linked to sleep problems, overall screen time, and violent and fastpaced content which activates dopamine and the reward pathways. Early and prolonged exposure to violent content is also linked to risk for antisocial behavior and decreased prosocial behavior. Psychoneurological effects: addictive screen time use decreases social coping and involves craving behavior which resembles substance dependence behavior. Brain structural changes related to cognitive control and emotional regulation are associated with digital media addictive behavior. A case study of a treatment of an ADHD diagnosed 9-year-old boy suggests screen time induced ADHD-related behavior could be inaccurately diagnosed as ADHD. Screen time reduction is effective in decreasing ADHD-related behavior. Conclusions: Components crucial for psychophysiological resilience are none-wandering mind (typical of ADHD-related behavior), good social coping and attachment, and good physical health. Excessive digital media use by children and adolescents appears as a major factor which may hamper the formation of sound psychophysiological resilience

Eur Child Adolesc Psychiatry. 2017 Dec;26:1483-99.

MENTAL HEALTH PROBLEMS IN AUSTRIAN ADOLESCENTS: A NATIONWIDE, TWO-STAGE EPIDEMIOLOGICAL STUDY APPLYING DSM-5 CRITERIA.

Wagner G, Zeiler M, Waldherr K, et al.

This is a nationwide epidemiological study using DSM-5 criteria to assess the prevalence of mental disorders in a large sample of Austrian adolescents between 10 and 18 years including hard-to-reach samples. A sample of 3615 adolescents from four cohorts (school grades 5, 7, 9, 11; age range 10-18 years) was recruited from 261 schools, samples of unemployed adolescents (n = 39) and adolescents from mental health institutions (n = 137) were added. The Youth Self-Report and SCOFF were used to screen for mental health problems. In a second phase, the Childrens' Diagnostic Interview for Mental Disorders was used to make point and lifetime psychiatric diagnoses. Mental health service use was also assessed. Point prevalence and lifetime prevalence rates for at least one psychiatric disorder were 23.9% and 35.8%. The highest lifetime prevalence rates were found for anxiety disorders (15.6%), neurodevelopmental disorders (9.3%; ADHD 5.2%) and depressive disorders (6.2%). Forty-seven percent of adolescents with a lifetime psychiatric disorder had a second diagnosis. Internalising disorders were more prevalent in girls, while neurodevelopmental disorders and disruptive, impulse control and conduct disorders were more prevalent in boys. Of those with a lifetime psychiatric disorder, 47.5% had contacted mental health services. Of the residual 52.5% who had not contacted mental health services, 18.1% expressed an interest in treatment. DSM-5 mental health disorders are highly prevalent among Austrian adolescents. Over 50% had or were interested in accessing treatment. Early access to effective interventions for these problems is needed to reduce burden due to mental health disorders

Eur J Gen Pract. 2016 Sep;22:196-202.

**GPS'** EXPERIENCES WITH ENHANCED COLLABORATION BETWEEN PSYCHIATRY AND GENERAL PRACTICE FOR CHILDREN WITH **ADHD**.

Hassink-Franke LJ, Janssen MM, Oehlen G, et al.

**BACKGROUND**: Most general practitioners (GPs) do not feel comfortable with diagnosing and treating children with attention deficit hyperactivity disorder (ADHD). This is problematic since ADHD is a prevalent disorder and an active role of GPs is desired. In the Netherlands a collaborative ADHD programme was established, comprising of shortened diagnostic assessment in specialized mental healthcare followed by psycho-education in mental healthcare and pharmacological treatment by pre-trained GPs.

**OBJECTIVES**: To explore the experiences of GPs regarding the diagnosis and treatment of children with uncomplicated ADHD within this programme.

**METHODS**: Semi-structured interviews with 15 GPs were conducted. The GPs participated in an evaluation of the collaborative ADHD programme. Data was analysed using the principles of constant comparative analysis.

**RESULTS**: Most participating GPs expressed reluctance to diagnose ADHD themselves. The reluctance was due to a lack of time, knowledge and experience. The GPs welcomed the collaborative programme because it met their need for both quick and adequate diagnosis by a specialist. Furthermore, an online ADHD course, offered by the programme, gave them the confidence to start and monitor ADHD medication. Finally, they appreciated the possibility of consulting a specialist when necessary.

**CONCLUSION**: GPs preferred that ADHD was diagnosed by a specialist. In the context of the ADHD collaborative programme, they felt competent and comfortable to start and monitor medication in children with uncomplicated ADHD. Key Messages Within a collaborative ADHD programme for children, participating GPs were positive about a quick and specialist diagnostic process within secondary care. After an online course, GPs felt confident to start and monitor ADHD medication in children with uncomplicated ADHD. GPs were content about the collaboration between primary and secondary care

Eur J Clin Nutr. 2018;1-7.

DIETARY PATTERNS ARE ASSOCIATED WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER (ADHD) SYMPTOMS AMONG PRESCHOOLERS IN MAINLAND CHINA.

Yan S, Cao H, Gu C, et al.

**BACKGROUND/OBJECTIVES**: To identify the major dietary patterns among preschoolers and assess the relation of major dietary patterns to attention-deficit/hyperactivity disorder (ADHD).

**SUBJECTS/METHODS**: A cross-sectional survey was conducted comprising a large sample of 14,912 children aged 3-6 years old in Ma'anshan city of Anhui Province in China. A semi-quantitative food frequency questionnaire and the 10-item Chinese version of the Conners' abbreviated symptom questionnaire were administered to assess usual dietary intakes and ADHD. Social-demographic information was also collected. Major dietary patterns were identified by principal components analysis. Logistic regression was employed to explore the association of dietary patterns with ADHD.

**RESULTS**: Five dietary patterns were identified explaining 47.96% of the total diet variation. The "processed" dietary component was the principal pattern that explained the higher percentage of variability, 24.69%. After controlling for potential confounders, preschoolers in the top quintile of the "processed" (odds ratio (OR) = 1.56, 95% confidence interval (CI): 1.31-1.86) and "snack" (OR = 1.76, 95% CI = 1.49-2.07) dietary pattern score had greater odds for having ADHD symptoms compared with those in the lowest quintile. Lowest scores on the "vegetarian" were associated with significantly a higher likelihood of indications of ADHD symptoms (OR = 0.67, 95% CI = 0.56-0.79).

**CONCLUSIONS**: This study showed that preschoolers tend to choose unhealthy dietary pattern in Ma'anshan, China. "Processed" and "snack" dietary patterns were significantly and positively correlated with ADHD symptoms, while "vegetarian" dietary patterns were negatively correlated with ADHD symptoms

Eur Neuropsychopharmacol. 2017;27:S286-S287.

A GENOME WIDE SIBLING TRANSMISSION DISEQUILIBRIUM ANALYSIS WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER IN KOREAN YOUTHS.

Kang Y, Kweon K, Shin E-S, et al.

**Background**: We aimed to explore the genetic underpinnings of Attention-Deficit/Hyperactivity Disorder (ADHD) by sibling transmission disequilibrium test (sib-TDT).

**Methods**: Twenty-seven youths with ADHD (age  $8.4 \pm 1.8$ , 22 boys) and their unaffected siblings (age  $9.1 \pm 2.2$ , 13 boys) were recruited through the Department of Psychiatry at the Asan Medical Center, Seoul, Korea. Diagnosis of children and their siblings was determined by the Diagnostic and Statistical Manual of Mental Disorders Fourth Edition (DSM-IV) and the Korean version of Schedule for Affective Disorders and Schizophrenia for school age children - Present and Lifetime version (K-SADS-PL). Genotyping was performed using Illumina Affymetrix Axiom" KORV1.0-96 Array. Statistical analyses were divided into two steps: (1) We searched candidate single-nucleotide polymorphisms which were possibly linked with ADHD. (2) SNP clusters which included three or more candidate SNPs within 100Kb were identified.

**Results**: 432,934 autosomal SNPs were subjected to sib-TDT. No single polymorphism reached genomewide significance. Fourteen SNPs showed possible association with ADHD (p<0.001). Among them, three SNPs (Rs2981084, rs2291219, rs56780268) were on TERF1 and SBSPON gene on Chromosome'8.

**Discussion**: In this study, TERF1 and SBSPON gene showed possible association with ADHD. Due to the small sample size, further research with larger sample size is needed

.....

Eur Neuropsychopharmacol. 2017;27:S139.

CHILDHOOD MALTREATMENT AND ADULT ATTENTION DEFICIT HYPERACTIVITY DISORDER SYMPTOMS: A TWIN STUDY. Capusan AJ, Bendtsen P, Kuja-Halkola R, et al.

**Background**: Research indicates robust association between childhood maltreatment and risk for ADHD in children and adolescents. Though less studied, similar association has been described in adults. This study

was performed to investigate to which extent this association is consistent with a causal interpretation, or if it is better explained by confounding factors shared within families.

**Methods**: We used material from the population representative Swedish twin-registry, The Study of Twin Adults: Genes and Environment. About 18,000 adult twins (age 20-46) supplied retrospective sel-ratings of childhood maltreatment (i.e., emotional and physical neglect, physical and sexual abuse and witnessing family violence), and self-rated DSM-IV ADHD symptoms in adulthood. We analyzed data using linear regression and within twin pair design based on monozygotic (MZ) and dizygotic (DZ) twin'pairs.

**Results**: Childhood maltreatment was significantly associated with higher DSM-IV ADHD symptom scores in adults (regression coefficient: 0.40 standard deviations (SD), 95% confidence interval (CI) 0.37, 0.43). Within twin pair analysis showed decreasing but significant estimates for DZ (0.29, 95% CI 0.21, 0.36) and MZ (0.18, 95% CI 0.10, 0.25) twin pairs, which indicate that the association is partly explained by familial confounding and is partly causal.

**Discussion**: The association between childhood maltreatment and ADHD symptoms in adults were partly due to familial confounding, but results also support causal effects. Clinicians treating adults with ADHD should be aware of the association with childhood maltreatment and possible causality

.....

Eur Neuropsychopharmacol. 2017;27:S209.

POLYGENIC RISK SCORE AND FAMILY HISTORY INDEPENDENTLY PREDICT CONDUCT DISORDER IN ADHD.

#### Thapar A, Agha SS, Martin J, et al.

**Background**: Previously in children with ADHD, polygenic risk scores (PGRS) have been found to predict comorbid conduct disorder. The relative risk of ADHD is also elevated in first degree relatives of ADHD probands who have conduct disorder vs. those with ADHD alone. The extent to which PGRS provides information about ADHD risk beyond that provided by family history has not been investigated.

**Methods**: This analysis included 329 children with ADHD from the Cardiff ADHD study. Presence of Conduct Disorder was assessed using the Child & Adolescent Psychiatric Assessment (CAPA). PGRS derived from a published PGC ADHD meta-analysis were calculated in this sample as previously described. Family history of ADHD was based on presence of parental ADHD in childhood and the past six months, assessed using self-report questionnaires. Logistic regression analyses were employed to investigate whether PGRS and family history of ADHD (ADHD in parents) predicted conduct disorder. The interaction between these potential risk factors was then investigated.

**Results**: Within this ADHD sample, 15.8% of participants had a diagnosis of conduct disorder. Ninety-one individuals (27.7%) had at least one parent with ADHD. Both ADHD PGRS (r2=0.110, p=0.047) and family history (r2=0.026, p=0.028) were associated with conduct disorder. The interaction term was not significant (p=0.53), suggesting that PGRS and family history have independent, additive effects.

**Discussion:** ADHD PGRS and family history of ADHD appear to have independent effects on conduct disorder in those with ADHD. Few studies (of psychiatric and medical disorders) have looked at the overlap between family history and polygenic risk as yet and none have done so within ADHD. This study gives an indication as to how these different measures of genetic risk may be usefully combined to predict an especially severe subtype of ADHD-those with conduct disorder. These findings suggest that knowledge of genetic risk profile scores can provide additional risk information to that of family history

.....

Eur Neuropsychopharmacol. 2017;27:S208-S209.

POLYGENIC RISK SCORES FOR CLINICAL **ADHD** ARE ASSOCIATED WITH IMPAIRED EDUCATIONAL ACHIEVEMENT AND LOWER **IQ** IN CHILDREN AND ADULTS FROM THE GENERAL POPULATION.

Stergiakouli E, Martin J, Hamshere M, et al.

**Background**: High levels of ADHD symptoms during early childhood carry risk of worse academic performance at age 16 (Washbrook et'al. 2013) and can impact on employment and earnings in adulthood (Fletcher 2013). Polygenic score analysis was used to show that common risk alleles for clinical ADHD contribute to the risk of having higher ADHD symptoms in the general population (Martin et'al. 2014). We

used polygenic risk score analysis to investigate the contribution of common risk variants for clinical ADHD on educational performance and IQ in the general population.

**Methods**: Polygenic risk scores were calculated for Avon Longitudinal Study of Parents and Children (ALSPAC) participants (Boyd et'al. 2013, Fraser et'al. 2013) (8,365 children and 8,340 mothers) based on the results of a discovery sample, a genome-wide association study of 727 cases with ADHD diagnosis and 5,081 controls from Cardiff University (Stergiakouli et'al. 2012) and tested for association with IQ and educational outcomes in adolescence and adulthood. The QC procedures and ascertainment of the target and discovery samples have been described in detail previously (Stergiakouli et'al. 2012, Stergiakouli et'al. 2014). Educational achievement was assessed using results from Key Stage 3'national tests, externally marked GCSE examinations and the probability of sitting Key Stage 5'examinations in 6,385 children from ALSPAC. Mothers' educational achievement was measured by self-reported highest qualification obtained. We also performed exploratory mediation analysis of the relationship between ADHD polygenic risk scores and ADHD symptoms with educational and cognitive outcomes in ALSPAC children.

**Results**: ADHD polygenic scores on the children were associated with worst educational outcomes at the 3'time points tested; Key stage 3'scores ( $\beta$  =-1.4 (-2 to -0.8), p=2.3 +ù 10-6), capped GCSE points ( $\beta$  =-4 (-6.1 to -1.9), p=1.8 +ù 10-4) and reduced probability of sitting Key Stage 5 examinations (OR=0.9 (0.88 to 0.97), p=0.001). They were also associated with lower IQ scores at age 15.5 ( $\beta$  =-0.8 (-1.2 to -0.4), p=2.4+ù10-4). Maternal ADHD polygenic scores were associated with lower maternal IQ ( $\beta$  =-0.6 (-1.2 to -0.1), p=0.03) and lower maternal educational achievement ( $\beta$  =-0.09 (-0.1 to -0.06), p= 0.005). Mediation analysis indicated that the association of ADHD polygenic risk score with educational outcomes was mediated substantially but not entirely by IQ and to a lesser extent by earlier levels of ADHD.

**Discussion**: Using a population-based sample, we demonstrated that genetic risk for clinical disorder is relevant for children and adults from the general population irrespective of whether they reach diagnostic criteria for the disorder. High genetic loading for clinical ADHD is associated with increased risk of educational under-achievement and lower IQ in ALSPAC. Our study highlights the potential of population samples for investigating the full distribution of psychiatric and cognitive traits in large numbers of individuals without a disorder diagnosis. Further investigation is required to determine if children with subthreshold ADHD symptoms would benefit from appropriate interventions and support to achieve their potential in education

.....

Eur Neuropsychopharmacol. 2017;27:S258.

THE GENETIC OVERLAP BETWEEN SCHIZOPHRENIA AND CHILDHOOD PSYCHOPATHOLOGY.

#### Middeldorp CM, Nivard M, Gage S, et al.

**Background**: The onset of schizophrenia is often preceded by a broad range of psychiatric symptoms, starting during adolescence or even during childhood. We investigated whether this association is explained by pleiotropy, i.e., genetic effects that influence both schizophrenia and childhood and adolescent psychiatric symptoms.

**Methods**: Based on the recent PGC schizophrenia metaanalysis, polygenic risk scores (PRS), reflecting an individual's genetic risk for schizophrenia, were constructed for 1,953 children from the Netherlands Twin Register (NTR) and 5,665 children from the Avon Longitudinal Study of Parents And Children (ALSPAC). The association between the PRS and DSM-IV based measures of anxiety, depression, Attention Deficit Hyperactivity Disorder (ADHD), Oppositional Defiant Disorder/Conduct Disorder (ODD/CD) was analyzed at age 7, 10, 12 and 15 years. The results were meta-analyzed across cohorts.

**Results**: The results revealed an FDR-corrected significant association between the PRS and anxiety at age 10 and nominal significant associations for anxiety at age 7'and depression at age 7'and 10. A post hoc analysis revealed stronger associations between the PRS and internalizing disorders than between the PRS and externalizing disorders.

**Discussion**: In line with the earlier reported significant association between adult major depression and schizophrenia, these results suggest a common genetic etiology for schizophrenia and internalizing disorders. In contrast, genetic factors do not explain the association between externalizing disorders at childhood and the onset of schizophrenia later in life

Newsletter – ADHD marzo 2018

Eur Neuropsychopharmacol. 2017;27:S246.

GENETIC CONTRIBUTIONS TO CARDIOVASCULAR TOLERABILITY OF ADHD PHARMACOTHERAPY.

# Nurmi E, Seaman L, Laughlin C, et al.

**Background**: Common side effects of standard attentiondeficit/hyperactivity disorder (ADHD) pharmacotherapy include changes in cardiovascular (CV) profiles, complicating treatment and representing a source of serious adverse events. A recent study of over 700,000 subjects in the Denmark health registry found that individuals exposed to stimulants had a higher risk of CV events (hazard ratio 1.83), especially children (hazard ratio 2.20). Individual genetic background may help explain the variability in these side effects, facilitating the identification of those at risk and safe clinical treatment matching. We captured complete common variation across drug target and signaling pathways to examine genetic association with CV measures during common ADHD treatments.

Methods: During both acute (8 weeks) and long-term (14 months) treatment phases with the stimulant dexmethylphenidate (d-MPH), the a-2 agonist quanfacine, and a combination of both medications, we collected regular CV measures in the NIMH Translational Research to Enhance Cognitive Control (TRECC) sample of 202 children with ADHD (ages 7-"14, 80% Caucasian, 70% male). Blood pressure (BP) and heart rate (HR) were recorded at each of up to 24 visits, and serial EKGs were performed at 5'time points to assess medication-related cardiac changes, including QTc interval prolongation predisposing to cardiac arrhythmia. Results: All treatments were associated with short-term CV changes that normalize over time. The quanfacine group experienced lower tolerability and greater dropout than the d-MPH group, but in combination with d-"MPH, dropout rates were comparable to the d-MPH group. Despite theoretical concerns about CV risk with concomitant use of d-MPH and quanfacine, combination treatment appears to mitigate the side effects of both monotherapies. A rare genetic variant in CNR1 was associated with extreme diastolic blood pressure (BP) decrease on guanfacine (p=4.0 +ù10-6), while variants in CHRNA7 and SLC6A4 predicted large systolic BP increases with d-MPH (p=1.9 x10-5). Two independent variants in CHRNA7 and a rare allele of SLC6A2 predicted heart rate elevation on combination treatment (p<0.0005). No genetic influences on EKG measures were observed. Replication and cross-disorder validation of these findings was performed in two samples of children with autism spectrum disorder treated with methylphenidate and guanfacine respectively.

**Discussion**: Our results suggest that genetic background contributes to differential treatment response and that medication choice may be guided by genetic information in order to avoid serious adverse effects. Four plausible genes emerged as moderators of medication effects on CV function, and implicated variants may have functional effects as predicted by ENCODE data. While these results survive Bonferroni correction for multiple testing, their interpretation is limited by small sample sizes and warrants replication in independent samples and prospective studies. Our finding at the norepinephrine transporter replicates a prior published result; other findings are novel. Additionally, a genomewide screen that is under analysis is likely to reveal additional underlying targets not anticipated in candidate analyses

.....

Eur Neuropsychopharmacol. 2017;27:S287.

A GENOME-WIDE ASSOCIATION ANALYSIS OF ATTENTION-DEFICIT/HYPERACTIVITY DISORDER IN KOREAN YOUTHS.

#### Kweon K, Shin E-S, Joo YH, et al.

**Background**: Attention-Deficit/Hyperactivity Disorder (ADHD) is a highly heritable neurodevelopmental disorder. We aimed to explore the genetic underpinnings of attention deficit hyperactivity disorder (ADHD) in Korean youths by genome-wide association (GWA) analysis.

**Methods**: Participants were recruited through the Department of Psychiatry at the Asan Medical Center, Seoul, Korea. Diagnosis of ADHD was determined by the Diagnostic and Statistical Manual of Mental Disorders Fourth Edition (DSM-IV) and the Korean version of Schedule for Affective Disorders and Schizophrenia for school age children - Present and Lifetime version. (K-SADS-PL) Genotyping was performed using Illumina Affymetrix Axiom" KORV1.0-96 Array. Statistical analyses were divided into two steps: (1) We searched candidate single-nucleotide polymorphisms which possibly associated with ADHD. (2) SNP clusters which included three or more candidate SNPs within 100Kb were identified.

**Results**: In total, 162 subjects (89 cases: age 8.0 7 1.7, 67 boys and 73 controls: age 8.9 7 2.0, 40boys) and 526,448 SNPs were subjected to GWA analysis. No single polymorphism reached genome-wide

significance. Two hundred thirtyeight SNPs showed possible association with ADHD. (p<0.001) Furthermore, seven SNP clusters were identified. (Five clusters in chromosome 1, one in chromosome 3, and one in chromosome 11). Among them, 19 SNPs were on NEGR1. 30 SNPs were located on FNDC7, STXBP3, and AKNAD1. 7'SNPs were located on MAN1C1. 7'SNPs were on FAM76A and STX12. 3'SNPs were on GLIS1. 3'SNPs were on LINC00636.

**Discussion**: In this study, NEGR1, FNDC7, STXBP3, AKNAD1, MAN1C1, FAM76A, STX12, GLIS1, and LINC00636 genes might be related to ADHD. Due to the limitation of sample size, further research to confirm these results is needed

.....

Eur Neuropsychopharmacol. 2017;27:S207-S208.

AN INTEGRATIVE APPROACH TO INVESTIGATE THE RESPECTIVE ROLES OF SINGLE-NUCLEOTIDE VARIANTS AND COPYnumber variants in attention-deficit/hyperactivity disorder.

Dos Santos ACF, De Ara+ijo LL, Belangero SI, et al.

**Background**: Attention-Deficit/Hyperactivity Disorder (ADHD) is the one of most common psychiatric disorders in childhood. Several studies have investigated ADHD genetic susceptibility suggesting a conexion among ADHD and some variants of small effect, as well as variants of small effects. As a subsequent step for identifying variants linked to ADHD susceptibility, it is important to understand how those variants interact with each other in order to increase risk for psychiatric disorders. The present investigation aimed to analyze rare and common variants contributing to the genetic architecture of ADHD.

**Methods**: We used data from different sources to analyze single-nucleotide variants (SNVs) and copynumber variants (CNVs). They were: a) exome findings for 30 brazilian trios where the children presented sporadic ADHD and SNP-arrays findings from 503 children with typical development from the High Risk Cohort for Psychiatric Disorders; b) results from the meta-analyses of GWAS in ADHD and 4'previously published CNV studies of ADHD involving Caucasian children/adolescent samples that are part of a public ADHD database (ADHDgene) c) brain expression data from public database and d) protein-protein interactions from the human interactome (PPI network analysis).

Results: Regarding to only probably deleterious variations, the results in ADHD trios showed 3'major patterns: (1)'de novo SNVs (25 variations) and inherited variations (134 - vary rare and 127 - rare); (2)'de novo CNVs (3 ins/del) and inherited variations (7 inherited from the father and 3'inherited from the mother); and (3)'only inherited variations. Comorbidities were more two times more frequent in cases with only inherited variants. After exploring the common and rare variant composition in our cases we selected genes that were both expressed in brain and have recurrent variations (SNVs or located in CNV regions) in our trio analysis or those from public data sets but not present in our controls (1048 genes). Topological and functional analyses of genes "in silico" in a protein-protein interaction network reveled genes related to synapse, cell adhesion, glutamatergic and serotoninergic pathways, confirming findings of previous studies and showing evidence of new genes in these pathways.

**Discussion**: Rare inherited variants play an important role in other neurodevelopment disorders. Therefore, we investigated ADHD trios exome and observed that it was necessary a combination of exclusively inherited variants or inherited plus few de novo variants. Interestingly, children who had de novo SNVs did not had de novo CNVs, and vice-versa, which corroborates with studies in other psychiatric diseases. Regarding functional analysis, our data highlighted biological functions significantly associated to ADHD. Promising results came up when only genes recurrent in at least two different analyses and their direct interactions on PPI databases have been used, since the connections in the neighborhood of these genes could show pathways with more confidence. The small sample size and admixed population such from Brazil brings particularities to the analyses. Thus we decide to use as much data integration as possible. Albeit our results confirm the disruption of pathways already associated to ADHD, it also confirms the complexity and heterogeneity of the disease, showing disruption in different genes can be conducing to the development of the disease

Eur Neuropsychopharmacol. 2017;27:S140-S141.

GENETIC LINKS BETWEEN SOCIAL-COMMUNICATION TRAITS, ADHD TRAITS AND CLINICAL ADHD DURING DEVELOPMENT.

St PB, Martin J, Stergiakouli E, et al.

**Background**: There is high comorbidity between autism spectrum disorders (ASD) and Attention Deficit Hyperactivity Disorder (ADHD) and population-based studies have shown complex symptom co-occurrence. At least some of these links are due to overlapping genetic influences. While trajectories for ASD symptoms are relatively stable during development however, trajectories for ADHD symptoms are more variable and only sometimes persistent into adulthood. This study was performed to investigate genetic links between ASD traits and ADHD traits in the general population, and ADHD disorder in a clinical sample, from a developmental perspective.

**Methods**: We studied social-communication difficulties (at ages 8, 11, 14 and 17 years; mother-reported Social and Communication Disorders Checklist, SCDC) and combined hyperactive-impulsive/inattentive symptoms (ages 7, 8, 10, 12, 13 and 17 years; mother-reported Strength and Difficulties Questionnaire, SDQ) in 5,680 children from a UK population-based birth cohort (Avon Longitudinal Study of Parents and Children, ALSPAC). Traits were rank transformed to normality, and genome-wide analyses carried out using 1000G imputed data in ALSPAC children. Genetic correlations within ALSPAC were assessed with Genome-Wide Complex Trait Analysis (GCTA). Genetic links between these traits and clinical ADHD (2,096 trios, 3,470 cases, 11,494 controls, based on available ADHD PGC GWAS summary statistics) were analysed using LD Score Regression (LDSC).

Results: There were genetic links between socialcommunication difficulties and ADHD traits throughout development, despite considerable variation in GCTA heritability (SCDC GCTA-h2: 0.08 to 0.45; SDQ GCTA-h2: 0.11 to 0.28). Irrespective of when social-communication difficulties were assessed, we observed, on average, smaller genetic correlations between these phenotypes and ADHD traits at 10 to 12 years, ranging between 0.10 to 0.56 (Pmin=0.02), while ADHD traits before and after this age showed stronger links, ranging between 0.41 to 1 (Pmin=8.0n10-5). We also found genetic correlations between clinical ADHD and social-communication difficulties at 8, 11 and 14 years, ranging between 0.33 and 0.75 (Pmino0.027), with some attenuation at 17 years (r=0.22, P=0.14). Findings were confirmed through polygenic score analysis in an ADHD PGC subsample (725 cases, 5081 controls; adjusted-R2 0.19%, P 0.004), based on a GWAS of social-communication difficulties in ALSPAC. As a positive control, we also confirmed genetic correlations between clinical ADHD and SDQ-assessed ADHD traits throughout development, ranging between 0.49 and 0.86 (all P<0.05).

**Discussion**: In summary, our findings support shared common genetic influences between social-communication difficulties and ADHD traits in the general population, as well as clinically-diagnosed ADHD, but suggest that detectable genetic overlaps may depend on developmental'stage

.....

Eur Neuropsychopharmacol. 2017;27:S243-S244.

ANXIETY, ADHD, AND EPILEPSY IN A MALE PATIENT WITH PATHOGENIC PCDH19 GENE VARIANT MOSIACISM.

Soden S. Thiffault I. Black B. et al.

Background: PCDH19 encodes protocadherin-19, a calcium dependent cell adhesion molecule expressed throughout the central nervous system, associated with brain development and synaptogenesis. Through a mechanism known as cellular interference, females with heterozygous PCDH19 variants develop early infantile epileptic encephalopathy-9 (EIEE9, OMIM 300088), also known as epilepsy and mental retardation restricted to females (EFMR), while carrier males are usually affected only by psychiatric or behavioral symptoms. EIEE9, is characterized by early normal development followed by febrile and temperature-induced seizures that tend to occur in clusters and may resemble Dravet syndrome. The phenotype arises in heterozygous females who have two populations of neurons: wild type, and PCDH19-Hemizygous males who have a homogeneous PCDH19-population of neurons remain carriers, however mosiacism has the potential to confer susceptibility to the EIEE9 phenotype in males.

**Methods**: A six year old male with obsessive compulsive symptoms, ADHD, and epilepsy was enrolled in a genome sequencing program for diagnosis of monogenic disorders. The patient had onset of seizures at 9-months. He has been on multiple medications for seizures, and initially they were refractory to treatment.

Anxiety based behavioral issues emerged by age 3. Obsessive compulsive features subsequently became predominant. Exome sequencing was performed on an Illumina HiSeq 2500 with 2 x 100 nucleotide sequences. Sequence was aligned to the human reference 37 and variants were detected and genotyped with the Genome Analysis Toolkit (GATK) version 1.6. Variants were annotated with the Rapid Understanding of Nucleotide variant Effect Software (RUNES'v1.0).

**Results**: The patient was identified with a truncating mutation in the PCDH19 gene, c.605C>A (p.Ser202Γêù). The variant was presumed de novo, as it was not detected in the patient mother. The patient appeared to have an admixure of the variant and normal nucleotides at this position, which would be atypical of a hemizygous male. Sanger sequencing confirmed that the variant was present in approximately 50% of the lymphocyte derived DNA sample. The patient was confirmed to have an XY karyotype, eliminating Kleinfelter Syndrome as an explanation for the admixure. PCDH19 variant mosiacism was determined to be the etiology of this patient epilepsy and neuropsychiatric symptoms.

**Discussion**: The increased use of next generation sequencing diagnostic tests has resulted in a rapidly expanding phenotype for many genes associated with neuropsychiatric disorders. In the era of phenotypically driven serial gene testing, patients with atypical features for a particular genetic disorder were often undiagnosed. However, the capacity of whole exome and whole genome sequencing (WES/WGS) to detect pathogenic changes in all genes, enables clinicians and researchers to quickly diagnose such patients. This case illustrates an unusual case of a male presenting with both psychiatric symptoms and a femalespecific form of epilepsy secondary to PCDH19 mosiacism

.....

Eur Neuropsychopharmacol. 2017;27:S150.

# FIRST RESULTS FROM THE CENSUSADHD STUDY: LARGE-SCALE MEDICATION BASED RECRUITMENT FOR ADHD. Mediand S

**Background**: Following from the recent successes of medication based recruitment strategies in adult psychiatric diseases we have been have been using this technique to recruit a large Australian cohort of pediatric ADHD cases. We hypothesized it would be possible to recruit a highly affected ADHD cohort via this mechanism as there is strong monitoring of the prescription of ADHD medications in Australia. These medications can only been prescribed by specialist Psychiatrists and Pediatricians, and prescriptions for these medications under the national health care system (Medicare) require secondary authorizations. Moreover, only 30% of children meeting criteria for ADHD are prescribed medication.

**Methods**: Within the censusADHD study, children aged 6-11 with three or more prescriptions for ADHD medications were identified by the Department of Human Services (DHS) based on Pharmaceutical Benefits Scheme records. To notify potential participants of the study, DHS sent the parents/caregivers of children meeting these criteria a letter describing the study and provide a url link for the study information and consent pages. Caregivers who choose to participate then complete in-depth online questionnaires providing information about their child behavior, treatment history, medication effectiveness and side effects, education history and performance. The caregivers also provide information about their own stress levels and the impact of ADHD on their financial, emotional and occupational wellbeing.

**Results**: In the first four weeks of the study, 1,558 parents of children with ADHD signed up for the study and 1,297 had finished the online questionnaires. Of the cases 78% were male; 75% presented as combined type, 19% as predominantly inattentive and 6% as predominantly hyperactive. Consistent with previous twin and family studies, of those families with two or more children, 28% had reported more than one child with ADHD. Furthermore, a history of childhood ADHD or attention problems was reported for 29% of the mothers and 50% of the fathers. A history of ADHD was reported at least one parent in 64% of families and both parents in 20% of families.

**Discussion**: Our study demonstrates that in countries with strictly regulated prescribing of ADHD medications, prescription based recruitment is a feasible and cost effective method of recruiting relatively large cohorts. In addition, these preliminary data demonstrate the importance of collecting phenotype data from parents of children with ADHD and the implications this may have for trio type designs. Challenges and considerations of using this recruitment design for studying childhood psychiatric disorders and the implications for genome wide association studies will be discussed

Newsletter – ADHD marzo 2018

Eur Neuropsychopharmacol. 2017.

EFFECT OF TOBACCO SMOKING ON FRONTAL CORTICAL THICKNESS DEVELOPMENT: A LONGITUDINAL STUDY IN A MIXED COHORT OF ADHD-AFFECTED AND -UNAFFECTED YOUTH.

#### Akkermans SEA, Van RD, Rommelse N, et al.

Smoking rates are particularly high during adolescence and young adulthood, when the brain is still undergoing significant developmental changes. Cross-sectional studies have revealed altered brain structure in smokers, such as thinner frontal cortical areas. Attention-deficit/hyperactivity disorder (ADHD) increases the risk of becoming nicotine-dependent, and has also been associated with abnormalities in frontal gray matter structure. The present study examines the relationships between smoking, cortical thickness and ADHD symptoms in a longitudinal design that compares adolescent and young adult smokers (n=44: 35 ADHD-affected) and non-smokers (n=45; 32 ADHD-affected) on frontal cortical thickness. Average frontal cortical thickness was estimated through structural magnetic resonance imaging (MRI) at two time points (mean ages 17.7 and 21.1 years), on average 3.4 years apart. Smokers had a 2.6% thinner frontal cortex than non-smokers and this difference was not explained by ADHD or other confounding factors. The rate of cortical thinning across the 3.4-year MRI measurement interval was similar in the total group of smokers compared to non-smokers. However, speeded thinning did occur in smokers who had started regular smoking more recently, in between the two measurements. These novel regular smokers did not differ significantly from the non-smokers at baseline. This suggests that the thinner frontal cortex was not a predisposing factor but rather a consequence of smoking. Although smokers had more ADHD symptoms overall, smoking did not influence the developmental course of ADHD symptoms

.....

Eur Neuropsychopharmacol. 2017;27:S141.

SHARED GENETIC EFFECTS BETWEEN CLINICAL ADHD AND SMOKING, ALCOHOL AND BREASTFEEDING IN MOTHERS FROM THE GENERAL POPULATION.

Stergiakouli E, Martin J, Hamshere M, et al.

**Background**: Smoking and alcohol consumption during pregnancy have been suggested as possible risk factors for ADHD in children (Huizink and Mulder 2006). However, inferring causality has not been possible because the mother provides both the prenatal environment and genetic risk factors for ADHD. When employing a design that disentangles genetic effects from the prenatal environment, the increased risk for ADHD in children of mothers who smoked during pregnancy was attributed to shared genetic risk factors (Thapar et'al. 2009). We investigated if there are shared genetic effects between ADHD and smoking and alcohol consumption during pregnancy, as well as breastfeeding using polygenic risk score analysis in mothers from the general population.

**Methods**: ADHD polygenic risk scores were calculated for Avon Longitudinal Study of Parents and Children (ALSPAC) participants (Boyd et'al. 2013, Fraser et'al. 2013) (8,340 mothers). The analysis used as a discovery sample, a genome-wide association study of 727 cases with ADHD diagnosis and 5,081 controls from Cardiff University (Stergiakouli et'al. 2012). Association of scores with smoking status and alcohol consumption before pregnancy and during the first trimester was tested in ALSPAC. Scores were also tested for association with breastfeeding status at 2'months postnatally. The QC procedures and ascertainment of the target and discovery samples have been described in detail previously (Stergiakouli et'al. 2012, Stergiakouli et'al.'2014).

**Results**: Higher genetic risk for ADHD, as indicated by polygenic scores, was associated with higher odds of smoking before pregnancy (OR=1.05 (1.01 to 1.1), p=0.03, N=7,530) and higher odds of continuing to smoke during the first trimester of pregnancy (OR=1.08 (1.03 to 1.15), p=0.002, N=7,543). However, there was no evidence of association with alcohol consumption both before pregnancy (OR=0.99 (0.91 to 1.08), p=0.93, N=7,543) and during the first trimester (OR=0.98 (0.94 to 1.03), p=0.5, N=7,525). Higher ADHD polygenic score was also associated with increased odds of the mother not breastfeeding at 2'months after the birth of the child (OR=1.06 (1.01 to 1.11), p=0.03, N=6,604). Child characteristics could also be influencing a mother in her decision to breastfeed or not. For this reason, the association of maternal ADHD polygenic scores with breastfeeding were adjusted for the ADHD polygenic score of the child. This did not change the association (OR=1.06 (0.99 to 1.13), p=0.09, N=4,619), although the confidence intervals are wider due to the smaller sample size compared to the unadjusted analysis.

**Discussion**: Our results indicate that there are shared genetic effects between ADHD and life style choices, such as smoking during pregnancy and breastfeeding. This is the first time that this has been shown using adults from the general population that do not reach diagnostic criteria for the disorder. In addition, these results raise the possibility of dynastic effects of genetic factors being present. In this case, the mother not only transmits genetic risk for ADHD to her offspring but also exposes the child to environmental risk factors, both prenatally and postnatally, through her life style choices that are in turn influenced by her genetic risk for ADHD. Importantly, we cannot infer causality from these associations. This should be assessed in a formal causal inference framework using Mendelian Randomization, although the small amount of variance explained by ADHD polygenic scores poses methodological challenges

.....

Eur Neuropsychopharmacol. 2018 Mar;28:381-91.

ANTERIOR CINGULATE CORTEX GLUTAMATE AND ITS ASSOCIATION WITH STRIATAL FUNCTIONING DURING COGNITIVE CONTROL.

### Naaijen J, Lythgoe DJ, Zwiers MP, et al.

Attention-deficit/hyperactivity disorder (ADHD) is a neurodevelopmental disorder characterized by structural, functional and neurochemical alterations of the fronto-striatal circuits and by deficits in cognitive control. In particular, ADHD has been associated with impairments in top-down fronto-striatal glutamate-signalling. However, it is unknown whether fronto-striatal glutamate is related to cognitive control dysfunction. Here we explored whether and how anterior cingulate cortex (ACC) glutamate relates to striatal BOLD-responses during cognitive control. We used proton magnetic resonance spectroscopy to evaluate glutamate-tocreatine ratios in 62 participants (probands with ADHD n = 19, unaffected siblings n = 24 and typical controls n = 19, mean age = 20.4). Spectra were collected from the ACC and the dorsal striatum and glutamate-tocreatine ratios were extracted. Thirty-two participants additionally took part in a functional magnetic resonance imaging (fMRI) Stroop task to investigate neural responses during cognitive control. Given small sample sizes we report all effects with p < 0.10 along with effect sizes. ADHD subjects showed decreased glutamate-to-creatine ratios in the ACC (F = 3.81, p = 0.059,  $?p^2 = 0.104$ ; medium to large effect-size) compared with controls. Importantly, decreased ACC glutamate-to-creatine ratios were associated with increased striatal BOLD-responses during cognitive control (rho = -0.41, p = 0.019; medium effect-size), independent of diagnosis. Increased striatal responses tended to be associated with more errors during the task and more hyperactivity/impulsivity symptoms (rho = 0.34, p = 0.058 and rho = 0.33, p = 0.068. respectively); the latter two being correlated too (rho = 0.37, p = 0.037), all with medium effect sizes. Our results suggest that ACC glutamate in ADHD might be associated with striatal (dys)functioning during the Stroop task, supporting the role of fronto-striatal glutamate in cognitive contro

.....

Fam Syst Health. 2018 Mar;36:73-86.

PRACTICE PROCEDURES IN MODELS OF PRIMARY CARE COLLABORATION FOR CHILDREN WITH ADHD.

#### Moore JA, Karch K, Sherina V, et al.

**Introduction**: With nationwide movement toward an integrated medical home, evidence to support, compare, and specify effective models for collaboration between primary care and behavioral health professionals is essential. This study compared 2 models of primary care with behavioral health integration on American Academy of Pediatrics guideline adherence for attention-deficit/hyperactivity disorder (ADHD) assessment and treatment.

**Method**: We conducted a retrospective chart review of a random sample of children aged 6–13 years, seen for ADHD services in 2 primary care offices, 1 fully integrated model and 1 co-located service only model, comparing ADHD assessment and treatment practices. We used chi-square analyses and logistic regression modeling to determine differences by type of health care model.

**Results**: Among children with ADHD (n = 149), the integrated care model demonstrated higher rates of guideline adherence, more direct contact with schools, and more frequent behavioral observation during clinical encounters. Families in the integrated practice received more caregiver education on ADHD,

behavioral management training, and school advocacy, however, these associations did not remain after accounting for variance associated with onsite engagement with a psychologist. Practices were equivalent on use of medication and psychiatric consultation, although, more families in the integrated practice engaged with a psychologist and attended more frequent medication follow-up appointments than those in the colocated practice.

**Discussion**: This study is among the first to compare different levels of collaborative care on practice procedures. Understanding how we can best integrate between behavioral health and primary care services will optimize outcomes for children and families

.....

Front Human Neurosci. 2018 Mar;12.

RESTING-STATE BRAIN SIGNAL VARIABILITY IN PREFRONTAL CORTEX IS ASSOCIATED WITH ADHD SYMPTOM SEVERITY IN CHILDREN.

#### Nomi JS, Schettini E, Voorhies W, et al.

Atypical brain function in attention-deficit/hyperactivity disorder (ADHD) has been identified using both task-activation and functional connectivity fMRI approaches. Recent work highlights the potential for another measure derived from functional neuroimaging data, brain signal variability, to reveal insights into clinical conditions. Higher brain signal variability has previously been linked with optimal behavioral performance. At present, little is known regarding the relationship between resting-state brain signal variability and ADHD symptom severity. The current study examined the relationship between a measure of moment-to-moment brain signal variability called mean-square successive difference (MSSD) and ADHD symptomatology in a group of children (7–12 years old) with (n = 40) and without (n = 30) a formal diagnosis of ADHD. A categorical analysis comparing subjects with and without a clinical diagnosis of ADHD showed no differences in MSSD between groups. A dimensional analysis revealed a positive relationship between MSSD and overall ADHD symptom severity and inattention across children with and without an ADHD diagnosis. Specifically, this positive relationship was found in medial prefrontal areas comprising the default mode network. These results demonstrate a link between intrinsic brain signal variability and ADHD symptom severity that cuts across diagnostic categories, and point to a locus of dysfunction consistent with previous neuroimaging literature

Graefe's Archive for Clinical and Experimental Ophthalmology. 2018;1-8.

ATTENTION-DEFICIT/HYPERACTIVITY DISORDER CHILDREN EXHIBIT AN IMPAIRED ACCOMMODATIVE RESPONSE.

#### Redondo B, Vera J, Molina R, et al.

**Purpose**: Attention-deficit/hyperactivity disorder (ADHD) is one of the most common paediatric neurobehavioural disorders causing multiple functional impairments in children. Based on the relationship between the neural system that controls attention and ocular dynamics, the present study compares the magnitude and variability of accommodation between a group of non-medicated ADHD children and an agematched control group.

.....

**Methods**: The magnitude and variability of the accommodative response were objectively measured in 36 children using the WAM-5500 autorefractometer for 90 consecutive seconds at three static viewing distances (500, 40, and 20 cm). Participants were divided into ADHD (n = 18) or control (n = 18) groups based on clinically validated criteria.

**Results**: Children with ADHD exhibited higher lags of accommodation (p = 0.024), increasing at closer viewing distances, in comparison to the control group. Marginal statistical differences were found for the variability of accommodation (p = 0.066), with the ADHD group showing a trend towards higher variability. Our analysis showed that the magnitude and variability of accommodation did not vary over time between groups (p > 0.05).

**Conclusions**: Our data suggest that children with ADHD have a less accurate accommodative response. These results provide a new ocular index that could help to clarify the relationship between accommodative response and attentional deficits, which could have a direct impact on the academic, cognitive, and visual performance of ADHD children

.....

Health Expect. 2016 Oct;19:1084-97.

END-USER INVOLVEMENT IN A SYSTEMATIC REVIEW OF QUANTITATIVE AND QUALITATIVE RESEARCH OF NON-PHARMACOLOGICAL INTERVENTIONS FOR ATTENTION DEFICIT HYPERACTIVITY DISORDER DELIVERED IN SCHOOL SETTINGS: REFLECTIONS ON THE IMPACTS AND CHALLENGES.

Coon JT, Gwernan-Jones R, Moore D, et al.

**BACKGROUND**: The benefits of end-user involvement in health-care research are widely recognized by research agencies. There are few published evaluations of end-user involvement in systematic reviews.

**OBJECTIVES**: (i) Describe end-user involvement in a complex mixed-methods systematic review of ADHD in schools, (ii) reflect on the impact of end-user involvement, (iii) highlight challenges and benefits experienced and (iv) provide suggestions to inform future involvement.

**METHODS**: End-users were involved in all stages of the project, both as authors and as members of an advisory group. In addition, several events were held with groups of relevant end-users during the project.

**RESULTS**: End-user input (i) guided the direction of the research, (ii) contributed to a typology of interventions and outcomes, (iii) contributed to the direction of data analysis and (iv) contributed to the robustness of the syntheses by demonstrating the alignment of interim findings with lived experiences. Challenges included (i) managing expectations, (ii) managing the intensity of emotion, (iii) ensuring that involvement was fruitful for all not just the researcher, (iv) our capacity to communicate and manage the process and (v) engendering a sense of involvement amongst end-users.

**CONCLUSIONS**: End-user involvement was an important aspect of this project. To minimize challenges in future projects, a recognition by the project management team and the funding provider that end-user involvement even in evidence synthesis projects is resource intensive is essential to allow appropriate allocation of time and resources for meaningful engagement

.....

Health Soc Work. 2016 Aug;41:164-72.

THE SUBJECTIVE EXPERIENCES OF ATTENTION-DEFICIT/HYPERACTIVITY DISORDER OF CHINESE FAMILIES IN HONG KONG: CO-CONSTRUCTION OF MEANINGS IN MULTIPLE FAMILY GROUPS.

Wan ESF, Ma JLC, Lai KYC, et al.

The subjective experiences of Chinese children in Hong Kong with attention-deficit/hyperactivity disorder (ADHD) are underexplored. This article reports the results of a qualitative study that aims to understand the subjective experiences of children with ADHD in Hong Kong, taken from among a clinical sample of Chinese families with children struggling with ADHD who have participated in cross-disciplinary research of multiple family groups (MFG). The participating children revealed the subjective experiences of their struggle with the disorder in response to their parents' concern at a "press conference," one of the MFG activities, which underscored the importance of developing a new social work model to meet the multiple psychosocial service needs of these families. The article concludes with the discussion of the implications for the new model

.....

Hum Brain Mapp. 2016 Aug;37:2833-48.

RECIPROCAL WHITE MATTER ALTERATIONS DUE TO 16P11.2 CHROMOSOMAL DELETIONS VERSUS DUPLICATIONS.

Chang YS, Owen JP, Pojman NJ, et al.

Copy number variants at the 16p11.2 chromosomal locus are associated with several neuropsychiatric disorders, including autism, schizophrenia, bipolar disorder, attention-deficit hyperactivity disorder, and speech and language disorders. A gene dosage dependence has been suggested, with 16p11.2 deletion

carriers demonstrating higher body mass index and head circumference, and 16p11.2 duplication carriers demonstrating lower body mass index and head circumference. Here, we use diffusion tensor imaging to elucidate this reciprocal relationship in white matter organization, showing widespread increases of fractional anisotropy throughout the supratentorial white matter in pediatric deletion carriers and, in contrast, extensive decreases of white matter fractional anisotropy in pediatric and adult duplication carriers. We find associations of these white matter alterations with cognitive and behavioral impairments. We further demonstrate the value of imaging metrics for characterizing the copy number variant phenotype by employing linear discriminant analysis to predict the gene dosage status of the study subjects. These results show an effect of 16p11.2 gene dosage on white matter microstructure, and further suggest that opposite changes in diffusion tensor imaging metrics can lead to similar cognitive and behavioral deficits. Given the large effect sizes found in this study, our results support the view that specific genetic variations are more strongly associated with specific brain alterations than are shared neuropsychiatric diagnoses

.....

Hum Brain Mapp. 2018.

ANTERIOR INSULA HYPERACTIVATION IN ADHD WHEN FACED WITH DISTRACTING NEGATIVE STIMULI.

#### Vetter NC, Buse J, Backhausen LL, et al.

Patients with attention deficit hyperactivity disorder (ADHD) suffer from poor emotion regulation that might arise from problems in the distribution of attentional resources when confronted with emotional distractors. Previous studies investigating the neurocognitive basis of these problems remain inconclusive. Moreover, most of these studies did not exclude participants with comorbidity, particularly of conduct or oppositional defiant disorder. The aim of this study was to assess alterations in fronto-limbic activation in ADHD adolescents specifically during negative distractors in an emotional attention task. For this purpose, we used functional magnetic resonance imaging to assess 25 boys with noncomorbid ADHD and 25 typically developing (TD) boys while they performed an emotional attention task with positive, negative, and neutral emotional distractors. Boys with ADHD had increased activation relative to TD boys specifically during the negative valenced stimuli in an emotional processing network comprising left anterior insula reaching into the inferior frontal gyrus. The findings suggest altered salience processing in ADHD of negative valenced emotional stimuli that may lead to higher distractibility in ADHD specifically when faced with negative emotional distractors

.....

Indian J Psychiatry. 2018;60:S136.

CLINICAL PROFILE OF PATIENTS ATTENDING CHILD GUIDANCE CLINIC: A FIVE YEAR RETROSPECTIVE STUDY FROM NORTH INDIA.

#### Arya S, Sethi S.

**Introduction**: About 10-20% of children and adolescent are affected by mental health problems. Despite such high prevalence rates, mental health needs of this group remains neglected, especially in lower and middles income countries. To address this a number of initiatives have been taken in India. This study aims to highlight the clinical profile of patients attending a child guidance clinic (CGC) in North India over a period of five years.

**Methods**: Records of patients attending CGC in last five years from 2012-2016 were retrieved and relevant socio-demographic and clinical details were noted down. Frequency analysis was done using SPSS 19. **Results**: A total of 2165 patients were registered over the five years. We were able to obtain data from 1706 records (79%). Majority were male (69%), between 5-15 years (77%), accompanied by either parent (83%), from rural background (55%), with ADHD being the most common diagnosis (2. 1%). The trends shown point towards increasing attendance in the CGC over this period as well as increased consultation for ADHD

Indian J Psychiatry. 2018;60:S142-S143.

ANALYSIS OF SIBLING RELATIONS IN CHILDREN WITH ATTENTION DEFCIT HYPERACTIVITY DISORDER.

# Nayak AS, Saurabh KH, Parkar SR, et al.

**Introduction**: Sibling relationships are often among an individual's longest lasting relationships. Siblings affect each other's development by being source of help, emotional support and companionship. Children with ADHD could be at higher risk of poor sibling relation because of their impaired interactions due to attention defcit. These affected sibling relationships could also lead to non-compliance and family conficts. Hence this study was undertaken.

Aims and Objectives: To study the quality of sibling relationship in children with ADHD and to compare it with normal controls Methodology: The present study was conducted at a child guidance clinic of a tertiary hospital after taking ethical clearance. 30 children diagnosed to have ADHD and 30 normal controls between the ages of 5 to 12 years, who had at least 1 live sibling; were recruited for the study. The parent rated version of the sibling relationship questionnaire (SRQ) was used to assess the quality of sibling relations in the 4 broad domains of warmth/closeness, relative status/power, rivalry and confict and several other subdomains. Unpaired student t test was used to compare the scores on the SRQ between the 2 groups.

**Results and Conclusion**: Our study showed lower levels of warmth in the ADHD group (p < 0. 05) as compared to the controls. The other 3 domains showed no significant difference. When the subdomains were analyzed, we found higher levels of affection, prosocial behavior and competition in the control group (p < 0. 05). Maternal partiality was seen less with children with ADHD (p < 0. 05). Our study concludes that sibling relations of children with ADHD are significantly strained as compared to normal children. Early identification and intervention should be carried out to improve the outcome in ADHD children

.....

Indian J Psychiatry. 2018;60:S77-S78.

PREVALENCE OF ATTENTION DEFCIT HYPERACTIVITY DISORDER AND IT'S COMORBIDITIES.

#### Suryaprabha B, Sireesha, Prasad HG.

**Introduction**: ADHD is one of the most common chronic behavioral disorder among children characterised by persistent hyperactivity, impulsivity and inattention. It effects multiple domains child's life causing significant impairment which is carried forward into adolescent and adulthood Hence it is important to diagnose and treat ADHD to prevent defects in overall functioning. It is often associated with multiple comorbiditis and optimal and timely addressal of them is also important

**Objectives of the study**: To study prevalence of ADHD among children aged 6-12 yrs of age. To study sociodemographic factors associated with study sample. To study comorbidities of ADHD subjects.

Inclusion Criteria: Parents of ADHD subjects who have given consent.

**Exclusion Criteria**: Parents who have not given consent Chronic physical illness Visual and hearing defects. **Place of study**: Tertiary hospital for women and child care Hyderabad.

Duration of study: November-December 2017.

**Methodology**: This is a cross-sectional study. Study involves children aged 6-11 years. All registered cases from psychiatric opd within this age limit are taken

**Sampling Technique**: convenience sampling. Consent is taken and confidentiality is maintained. ADHD-diagnosed by DSM 5 Separate Semi structured intake proforma for child and parent will be used to elicit birth and developmental milestones of children, history of substance abuse, educational qualifications of parents, family history of ADHD, mental illness and recent stressful life events. Semi structured proforma and Vanderbilt scale for assessment of comorbidities will be given to parents.

Analysis: SPSS software version 17. Results & conclusion: will be discussed at time of presentation

Indian J Psychiatry. 2018;60:S79.

A STUDY OF SOCIODEMOGRAPHIC PROFILE AND PSYCHIATRIC COMORBIDITIES IN ADOLESCENT PATIENTS WITH DELIBERATE SELF HARM: A CHART REVIEW.

## Indu CG, Alex S, Sathesh V.

**Background**: Suicide is a major public health concern and WHO estimates that nearly 900, 000 people worldwide die from suicide every year [1Adolescents constitute 21 per cent of the population of India. Hence study about adolescents got huge public importance.

**Aim**: The aim of this study was (1)To study the sociodemographic profile of Adolescent patients with Deliberate Self Harm. (2)To study the psychiatric morbidities in them.

**Materials and Methods**: This is a descriptive observational study done by chart review from July 2016 to July 2017 of adolescent patients with Deliberate Self Harm who attended Suicide prevention clinic, Department of Psychiatry at a Tertiary care center. Out of 57 adolescents attended the Suicide prevention clinic. 43 were included. Sociodemographic and clinical profiles were collected using the semi-structured proforma. The assessment of Suicide intent was done by Beck's suicide Intent Scale. Psychiatric comorbidity of these patients was assessed on Structured clinical interview for DSM-5. The data were tabulated and analysed using Descriptive statistics. Statistical Package for the social sciences(SPSS) Version 22 was used for analysis.

**Results**: Females studying in Higher secondary school outnumbered the males, majority under the age group of 16 and 17 years coming from nuclear family belonging to Above poverty line group. Most of them were of low intent with mixed personality traits followed by borderline traits and with other psychiatric morbidities such as adjustment disorders, conduct disorders, ADHD, Substance use disorders and no subjects fell under the classification of Non suicidal self injury.

**Conclusion**: Age group 16 and 17 were more vulnerable to deliberate self-harm and majority were females, with scolding as the main triggering factor. Majority was of low intent with borderline personality traits and adjustment disorders and no subjects involved under the classification of Non suicidal self injury

.....

Indian J Psychiatry, 2018:60:S162.

THE IMPACT OF ATTENTION DEFCIT HYPERKINETIC DISORDER ON RESIDUAL SYMPTOMS IN BIPOLAR DISORDER.

## Jhanda S, Grover S, Malhotra S.

**Aim**: This study aimed to evaluate the impact of comorbid Attention Defcit Hyperkinetic Disorder (ADHD) on residual symptoms among patients with Bipolar disorder (BD).

**Methods**: Patients aged 13-40 years with history of BD with ADHD (N=30) were compared to patients with BD without ADHD (N=69) for presence of residual affective symptoms during the remission phase of illness. **Results**: As compared to those without ADHD, patients of BD with ADHD had higher level of residual depressive symptoms in the form of total Hamilton Depression Rating Scale (HDRS) score (p-0. 001). Those with BD with ADHD had higher severity of depressed mood (p-0. 001), guilt (p=0. 03), suicidal behavior (p=0. 001), early insomnia (p=0. 01), impairment in work and activities (p=0. 01) and somatic anxiety (0. 03) on the HDRS. In terms of manic symptoms, higher severity was noted only for the symptom of irritability (p=0. 04) on the Young Mania Rating Scale (YMRS) in the BD with ADHD group.

**Conclusions**: Comorbid ADHD has negative impact on outcome of BD in terms of increased severity of subsyndromal symptoms that can negatively affect functionality

Indian J Psychiatry. 2018;60:S147-S148.

LENNAUX-GASTAUT SYNDROME PRESENTING WITH SYMPTOMS OF ADHD-A CASE REPORT.

## Pradhan M.

**Background**: Lennox-Gastaut syndrome is a form of severe epilepsy that begins in childhood. It is characterized by multiple types of seizures and intellectual disability. People with Lennox-Gastaut syndrome begin having frequent seizures in early childhood, usually between ages 3 and 5. The association of attention

defcit hyperactivity disorder can cause significant impact on the social life of affected individuals and their families. Clinical studies suggest that 30-40% of people with epilepsy also have ADHD.

**Aim and Objective**: to present the case of a patient of Lennox-Gastaut syndrome who presented with attention defcit and hyperactive symptoms.

**Material and Methods**: A 7 year old male child presented with the chief complaint of restlessness, moving around the house, fdgety behavior, episodes of self-injurious behavior. He was stubborn towards parents. the symptoms of 2 yrs duration with insidious onset and continuous course. The academic performance was poor and patient remained inattentive during studies. On ADHD checklist, he was found to have moderate level of hyperactivity. On medical evaluation and past treatment records, patient was found to be a diagnosed case of Lennox-Gastaut syndrome. the seizures started at the age of 1. 5 years. the episodes gradually increased in frequency and severity. Patient was prescribed methylphenidate and the antiepileptics were continued as advised. After 3 to 4 follow ups, in a span of 7 months, the hyperactive symptoms subsided.

**Conclusion**: ADHD is often under diagnosed in children. Its comorbidity with epilepsy is an add-on burden. So, early diagnosis and treatment is very important for prevention of long-term effects. As children diagnosed with ADHD often have significant difficulties in adolescence regardless of treatment, so early detection, diagnosis and treatment is very important for prevention of long-term adverse effects of ADHD

.....

Int J Dev Neurosci. 2017 Aug;60:86-93.

TYPE 1 DIABETES, COGNITION AND THE NEUROLOGIST: EXPLORING GO/NO-GO AND MAZE TASKS IN THE SEARCH FOR A PRACTICAL SCREENING TOOL.

Shinosaki JSM, Rossini JC, Jorge MLPM, et al.

**AIMS**: The objectives were to use inexpensive and easy-to-apply tasks in order to investigate the differences between type 1 diabetes mellitus (T1DM) patients and controls regarding attention and impulsivity, which are the basis for key-executive function components that are traditionally assessed using subjective, long and difficult to reproduce questionnaires. Additionally, we sought to correlate these differences with clinical characteristics, and to explore correlations between the tasks.

**METHODS**: We compared the scores of 20 T1DM patients with 20 controls. The sample population included both males and females, aged 12-15 years. They were tested using a Go/No-Go paradigm and a Maze task, and correlations were verified between the groups.

**RESULTS**: The T1DM group had more anticipatory answers (AA) in the Go/No-Go task (p <0.05), and made more direction changes in Mazes (p<0.01). There was a correlation between non-severe hypoglycemia and AA (p=0.01), as well as between severe hypoglycemia and the number of touches in Mazes' walls (p<0.05). Glycated hemoglobin (HbA1c)>9% correlated with a greater number of alleys in Mazes (p<0.05). The tasks' parameters were coherent among each test, and also between them.

**CONCLUSIONS**: We found indicators of inattention and impulsivity to be associated with T1DM, with inattention being closely related with hyperglycemia, and impulsivity being associated with hypoglycemia. Further research is needed to study diabetes-associated cognitive decline with more objective parameters, and to analyse the reliability and psychometric properties of the tasks proposed in this study

Int J Dev Neurosci. 2017 Aug;60:34-47.

METHYLPHENIDATE EFFECTS IN THE YOUNG BRAIN: FRIEND OR FOE?

Loureiro-Vieira S, Costa VM, de Lourdes BM, et al.

Attention deficit hyperactivity disorder (ADHD) is one of the most prevalent neuropsychiatry disorders in children and adolescents, and methylphenidate (MPH) is a first-line stimulant drug available worldwide for its treatment. Despite the proven therapeutic efficacy, concerns have been raised regarding the possible consequences of chronic MPH exposure during childhood and adolescence. Disturbances in the neurodevelopment at these crucial stages are major concerns given the unknown future life consequences. This review is focused on the long-term adverse effects of MPH to the brain biochemistry. Reports conducted with young and/or adolescent animals and studies with humans are reviewed in the context of long-term

consequences after early life-exposure. MPH pharmacokinetics is also reviewed as there are differences among laboratory animals and humans that may be relevant to extrapolate the findings. Studies reveal that exposure to MPH in laboratory animals during young and/or adolescent ages can impact the brain, but the outcomes are dependent on MPH dose, treatment period, and animal's age. Importantly, the female sex is largely overlooked in both animal and human studies. Unfortunately, human reports that evaluate adults following adolescent or child exposure to MPH are very scarce. In general, human data indicates that MPH is generally safe, although it can promote several brain changes in early ages. Even so, there is a lack of long course patient evaluation to clearly establish whether MPH-induced changes are friendly or foe to the brain and more human studies are needed to assess the adult brain changes that arise from early MPH treatment

.....

Int J Epidemiol. 2016 Dec;45:1987-96.

ACETAMINOPHEN USE IN PREGNANCY AND NEURODEVELOPMENT: ATTENTION FUNCTION AND AUTISM SPECTRUM SYMPTOMS.

Avella-Garcia CB, Julvez J, Fortuny J, et al.

**Background**: Acetaminophen is extensively used during pregnancy. But there is a lack of population-representative cohort studies evaluating its effects on a range of neuropsychological and behavioural endpoints. We aimed to assess whether prenatal exposure to acetaminophen is adversely associated with neurodevelopmental outcomes at 1 and 5 years of age.

**Methods**: This Spanish birth cohort study included 2644 mother-child pairs recruited during pregnancy. The proportion of liveborn participants evaluated at 1 and 5 years was 88.8% and 79.9%, respectively. Use of acetaminophen was evaluated prospectively in two structured interviews. Ever/never use and frequency of use (never, sporadic, persistent) were measured. Main neurodevelopment outcomes were assessed using Childhood Autism Spectrum Test (CAST), Conner's Kiddie Continuous Performance Test (K-CPT) and ADHD-DSM-IV form list. Regression models were adjusted for social determinants and co-morbidities.

**Results**: Over 40% of mothers reported using acetaminophen. Ever-exposed offspring had higher risks of presenting more hyperactivity/impulsivity symptoms [incidence rate ratio (IRR) = 1.41, 95% confidence interval (CI) 1.01-1.98), K-CPT commission errors (IRR = 1.10, 1.03-1.17), and lower detectability scores (coefficient beta = -0.75, -0.13--0.02). CAST scores were increased in ever-exposed males (beta = 0.63, 0.09-1.18). Increased effect sizes of risks by frequency of use were observed for hyperactivity/impulsivity symptoms (IRR = 2.01, 0.95-4.24) in all children, K-CPT commission errors (IRR = 1.32, 1.05-1.66) and detectability (beta = -0.18, -0.36-0.00) in females, and CAST scores in males (beta = 1.91, 0.44-3.38).

**Conclusions**: Prenatal acetaminophen exposure was associated with a greater number of autism spectrum symptoms in males and showed adverse effects on attention-related outcomes for both genders. These associations seem to be dependent on the frequency of exposure

.....

Int J Epidemiol. 2016 Dec;45:2009-17.

PARACETAMOL USE DURING PREGNANCY AND ATTENTION AND EXECUTIVE FUNCTION IN OFFSPRING AT AGE 5 YEARS. Liew Z, Bach CC, Asarnow RF, et al.

**Methods**: We studied 1491 mothers and children enrolled in the Danish National Birth Cohort (DNBC; 1996-2002). Prenatal paracetamol use was prospectively recorded in three telephone interviews. Trained psychologists assessed child's attention function using the Test of Everyday Attention for Children at Five (TEACh-5). Parents and preschool teachers completed Behaviour Rating Inventory of Executive Function (BRIEF) to assess executive functions. We estimated the differences of composite mean outcome scores, and odds ratios (OR) for subnormal attention or executive function (defined as 1 standard deviation below the mean), adjusting for maternal IQ, maternal mental health, indications for paracetamol use and other potential confounders.

**Results**: First trimester use of paracetamol was associated with poorer attention scores in childhood [mean difference -0.34, 95% confidence interval (CI) -0.63, -0.05 for overall attention, and -0.25, 95% CI -0.50, 0.01

for selective attention]. Children prenatally exposed to paracetamol were also at a higher risk for subnormal overall attention (OR = 1.5, 95% CI 1.0, 2.5), selective attention difficulties (OR = 1.5, 95% CI 1.0, 2.4), and parent-rated subnormal executive function (metacognition index, OR = 1.5, 95% CI 0.9, 2.3). The risks for subnormal overall attention or executive function were elevated with longer duration of paracetamol use in pregnancy.

**Conclusions**: We found some evidence that maternal paracetamol use during pregnancy was associated with poorer attention and executive function in 5-year-olds

.....

Int J Eating Disord. 2018;51:223-32.

CUE REACTIVITY, HABITUATION, AND EATING IN THE ABSENCE OF HUNGER IN CHILDREN WITH LOSS OF CONTROL EATING AND ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.

## Hilbert A, Kurz S, Dremmel D, et al.

**Objective**: Childhood loss of control (LOC) eating and attention-deficit/hyperactivity disorder (ADHD) are highly comorbid conditions and present with disordered eating behaviors, such as overeating. This study sought to delineate shared and specific abnormalities in physiological, cognitive-motivational, and behavioral components of food-specific impulsivity in children with LOC eating and ADHD. Specifically, children's reactivity and habituation to food and eating in the absence of hunger were examined.

**Methods**: Within this community-based study, four groups of 8-13-year-old children with LOC eating (n = 24), ADHD (n = 32), comorbid LOC eating/ADHD (n = 9), and matched controls (n = 34) received a standard laboratory test meal to establish satiety and were then exposed to their favorite snack food in a cue exposure/reactivity trial, while salivation and desire to eat were repeatedly assessed. Subsequently, they were offered a variety of snack foods ad libitum.

**Results**: Children with LOC eating, ADHD, and LOC/ADHD did not differ from controls in salivary reactivity and habituation to food cues. Children with LOC eating and ADHD showed greater cue reactivity of the desire to eat than controls, but groups did not differ in its longer-term increments. At free access, only children with LOC/ADHD consumed significantly more energy than controls. Longer-term increments of desire to eat predicted greater energy intake beyond LOC/ADHD group status.

**Discussion**: Desire to eat among children with comorbid LOC eating and ADHD was associated with overeating in the absence of hunger, which may contribute to excess weight gain. Delineation of the specific features of childhood LOC eating versus ADHD warrants further study

.....

Iranian Journal of Parasitology. 2017;13:147.

STUDY OF LATENT TOXOPLASMOSIS IN CHILDREN WITH ATTENTION DEFICIT/HYPERACTIVITY DISORDERS AND HEALTHY CHILDREN IN YAZD.

# Ghafourzadeh M, Zia-Ali N, Razavi H.

**Background**: Toxoplasmosis is one of the most common parasitic diseases worldwide which is caused by Toxoplasma gondii. Although estimated that one third of the world's population are infected with T. gondii, but the most common form of the disease is latent (asymptomatic). With reference to the hypothesis of association between central nervous system infections and different mental disorders. In this study the relationship between T. gondii infections and ADHD (attention deficit/hyperactivity disorders) was studied. Methods: In this case-control study, 100 serums of ADHD patients referred to psychological clinics in Yazd, Iran and 100 serum samples as matched were gathered. IgG specific antibodies against T. canis were detected using CLIA test (Chemiluminescence Immunoassay). Data were analyzed using parage 2 test, t-test and Fisher exact test.

**Results**: Over ally, 6% of the case samples and 2% of the control samples were seropositive for IgG specific antibodies to T. gondii; and the differences were not statistically significant (P>0.05).

**Conclusion**: The result of our study showed that there was no epidemiological relationship between the infection of T. gondii and the hyperactivity/attention deficit disorders (ADHD). However, considering the high titer of anti-Toxoplasma IgG antibody in children with ADHD, There may be a causal relationship between

toxoplasmosis and etiology Of ADHD. According to this study and more researches maybe we can present new methods for diagnosis, treatment and prevention of ADHD

.....

Iran J Psychiatr Behav Sci. 2017;11.

EFFECTIVENESS OF A VISUAL ATTENTION TRAINING PROGRAM ON THE REDUCTION OF ADHD SYMPTOMS IN PRESCHOOL CHILDREN AT RISK FOR ADHD IN ISFAHAN: A PILOT STUDY.

Joekar S, Amiri S, Joekar S, et al.

**Background**: Attention deficit hyperactivity disorder (ADHD) symptoms are difficult to treat. As ADHD is naturally a disorder of attention and related executive functions, attention training (ATT) has been considered as a treatment for the disorder. Although there are few studies investigating the utility of ATT in the ADHD population, published studies provide support for ATT in reducing the symptoms of ADHD.

**Objectives**: The aim of the current study was to examine the effects of training attention on ADHD symptoms in a group of preschool-aged children at risk for ADHD disorder. Methods: In this study, a group of 5-year-old children (n = 30) with ADHD symptoms were assigned randomly to either a traininggroup who participated in 11 sessions of visual attention training based on Pay Attention Program or a non-trained control group. Both versions of Child symptom inventory-4 (CSI-4) were employed to assess ADHD symptoms based on parent and teacher's rating. Also the accuracy and the continuous performance of children were examined with Tolouse-Pierron test. The Assessment was performed in three phases: (1) before, (2) after, and (3) one month after the termination of training.

**Results**: Results of the multivariate analysis of the covariance demonstrate that there was a significant difference (P < 0.05) in the decline of attention deficit symptoms between two groups based on teacher's rating at post-test. In addition, there was a significant decrease (P < 0.05) on the scores of omission error of Toulose- Pieron test at post-test and follow up for the training group. There was no significant reduction in hyperactivity symptoms in two groups.

**Conclusions**: It seems that the performance of children's attention with ADHD improves by visual attention training

.....

J Abnorm Child Psychol. 2017 Jul;45:947-58.

INTERRELATIONSHIPS AND CONTINUITIES IN SYMPTOMS OF OPPOSITIONAL DEFIANT AND CONDUCT DISORDERS FROM AGE 4 TO 10 IN THE COMMUNITY.

## Husby SM, Wichstrom L.

Childhood oppositional defiant disorder (ODD) has commonly been thought to increase the risk of conduct disorder (CD) in late childhood and adolescence. However, symptoms of CD may also emerge during preschool and middle childhood. The few studies that have examined whether ODD increases the risk of such early onset CD have produced equivocal results, potentially due to methodological issues. In this study, a community sample of Norwegian 4-year-olds (n = 1042, 49.9 % males) was examined bi-annually over four waves of data collection. Symptoms of ODD, CD, attention-deficit/hyperactivity disorder (ADHD), anxiety and depressive disorders were measured through interviews with parents and children using the Preschool Age Psychiatric Assessment and the Child and Adolescent Psychiatric Assessment. The results showed that at all ages, more symptoms of ODD predicted more symptoms of CD at the next age of examination even after adjusting for previous CD and comorbid conditions. The effect of previous ODD on CD two years later did not differ according to gender, SES, or parental cohabitating status at any point in time. There was modest homotypical continuity in symptoms of CD and moderate homotypical continuity in symptoms of ODD. Symptoms of ODD increased from age 4 to 8 and declined to age 10. In conclusion, symptoms of ODD increase the risk of early onset symptoms of CD. The continuity in symptoms of ODD, and to some extent CD, combined with an increased risk of early symptoms of CD forecasted by symptoms of ODD, underscore the importance of detection, prevention and treatment of behavioral disorders already in early childhood

J Abnorm Child Psychol. 2017 Jul;45:883-97.

# FACTORS ASSOCIATED WITH HEALTHY AND IMPAIRED SOCIAL FUNCTIONING IN YOUNG ADOLESCENTS WITH ADHD. Ray AR, Evans SW, Langberg JM.

There is variability in the extent to which adolescents with attention-deficit/hyperactivity disorder (ADHD) exhibit social impairment, as the same diagnosis does not necessarily entail impairment in the same area(s) of functioning. The current study entailed a cross-sectional examination of enhancers to healthy social functioning and risk factors to parent- and self-rated social impairment in 324 middle school youth (ages 10-14 years) with ADHD. A series of binary logistic regression analyses were conducted to evaluate a risk-resilience model for social functioning, including testing compensatory (i.e., main; buffering) and protective (i.e., interaction) effects of enhancers in the presence of identified risk factors. Youth conduct problems, youth depression, and negative parenting emerged as risk factors. Self-rated social acceptance, activity participation (breadth and intensity), and parent involvement were enhancers of healthy social functioning. Of these enhancers, activity participation (breadth and intensity) and parent involvement showed buffering effects against the negative impact of the risk factors on social functioning. None of the enhancers displayed protective effects. The findings of this study enhance our understanding of the social functioning of young adolescents with ADHD, who comprise an understudied population relative to younger children with similar problems

.....

J Abnorm Child Psychol. 2017 Jul;45:911-20.

ACUTE STIMULANT TREATMENT AND REINFORCEMENT INCREASE THE SPEED OF INFORMATION ACCUMULATION IN CHILDREN WITH ADHD.

## Fosco WD, White CN, Hawk LW, Jr.

The current studies utilized drift diffusion modeling (DDM) to examine how reinforcement and stimulant medication affect cognitive task performance in children with ADHD. In Study 1, children with (n = 25; 88 % male) and without ADHD (n = 33; 82 % male) completed a 2-choice discrimination task at baseline (100 trials) and again a week later under alternating reinforcement and no-reinforcement contingencies (400 trials total). In Study 2, participants with ADHD (n = 29: 72 % male) completed a double-blind, placebo-controlled trial of 0.3 and 0.6 mg/kg methylphenidate and completed the same task utilized in Study 1 at baseline (100 trials). Children with ADHD accumulated information at a much slower rate than controls, as evidenced by a lower drift rate. Groups were similar in nondecision time and boundary separation. Both reinforcement and stimulant medication markedly improved drift rate in children with ADHD (ds = 0.70 and 0.95 for reinforcement and methylphenidate, respectively); both treatments also reduced boundary separation (ds = 0.70 and 0.39). Reinforcement, which emphasized speeded accuracy, reduced nondecision time (d = 0.37), whereas stimulant medication increased nondecision time (d = 0.38). These studies provide initial evidence that frontline treatments for ADHD primarily impact cognitive performance in youth with ADHD by improving the speed/efficiency of information accumulation. Treatment effects on other DDM parameters may vary between treatments or interact with task parameters (number of trials, task difficulty). DDM, in conjunction with other approaches, may be helpful in clarifying the specific cognitive processes that are disrupted in ADHD, as well as the basic mechanisms that underlie the efficacy of ADHD treatments

.....

J Abnorm Child Psychol. 2017 Jul;45:857-69.

ADHD SYMPTOMS IN POST-INSTITUTIONALIZED CHILDREN ARE PARTIALLY MEDIATED BY ALTERED FRONTAL EEG ASYMMETRY.

# Frenkel TI, Koss KJ, Donzella B, et al.

Individual differences in the propensity for left versus right frontal electroencephalogram (EEG) asymmetry may underlie differences in approach/withdrawal tendencies and mental health deficits. Growing evidence suggests that early life adversity may shape brain development and contribute to the emergence of mental health problems. The present study examined frontal EEG asymmetry (FEA) following the transition to family care in children adopted internationally from institutional care settings between 15 and 36 months of age (N

= 82; 46 female, 36 male). Two comparison groups were included: an international adoption control consisting of children adopted from foster care with little to no institutional deprivation (N = 45; 17 female, 28 male) and a post-adoption condition control consisting of children reared in birth families of the same education and income as the adoptive families (N = 48; 23 female, 25 male). Consistent with evidence of greater approach and impulsivity-related behavior problems in post-institutionalized (PI) children, PI status was associated with greater left FEA than found in the other two groups. In addition, left FEA served as a mediator between institutionalization and age 5 ADHD symptoms for girls. Age at adoption and other preadoption factors were examined with results suggesting that earlier adoption into a supportive family resulted in a more typical pattern of brain functioning. Findings support the idea that the capacity of brain activity to evidence typical functioning following perturbation may differ in relation to the timing of intervention and suggest that the earlier the intervention of adoption, the better

.....

J Abnorm Child Psychol. 2017 Jul;45:871-82.

MOTHER-CHILD RELATIONSHIP IN YOUTHS WITH ATTENTION-DEFICIT HYPERACTIVITY DISORDER AND THEIR SIBLINGS.

#### Chang JP, Gau SS.

Despite impaired mother-child interactions noted in youth with attention-deficit/hyperactivity disorder (ADHD), there is no such information for their siblings. This study aimed to test whether the affected and unaffected siblings, like youth with ADHD, also encountered impaired mothering and mother-child relationships as compared to typically developing youth (TD). The sample consisted of 122 probands (107 males, 87.7 %), aged 10-16, with DSM-IV ADHD, 44 affected (26 males, 59.1 %) and 78 unaffected (28 males, 35.9 %) siblings, and 122 TD youth. Both participants and their mothers received psychiatric interviews (K-SADS-E) about the participants and reported maternal parenting style, mother-child interactions and child behavioral problems at home. Based on both reports, probands with ADHD and affected siblings (only youth report) had more impaired relationships, more behavioral problems at home, and less perceived family support than unaffected siblings and TD youth. Probands with ADHD had higher maternal authoritarian control than unaffected siblings. The findings suggest that impaired mothering, mother-child interactions, and family support are related to the presence of ADHD diagnosis in both probands and their affected siblings

.....

J Abnorm Child Psychol. 2017 Jul;45:899-910.

EXECUTIVE FUNCTIONING AND ENGAGEMENT IN PHYSICAL AND RELATIONAL AGGRESSION AMONG CHILDREN WITH ADHD.

#### McQuade JD, Breaux RP, Miller R, et al.

Although evidence suggests that executive functioning (EF) impairments are implicated in physically aggressive behavior (e.g., hitting) these cognitive impairments have rarely been examined with regard to relational aggression (e.g., gossip, systematic exclusion). Studies also have not examined if EF impairments underlie the expression of aggression in children with attention-deficit/hyperactivity disorder (ADHD) and if child gender moderates risk. Children with and without clinical elevations in ADHD symptoms (N = 124; ages 8-12 years; 48 % male) completed a battery of EF tests. Parent and teacher report of ADHD and oppositional defiant disorder (ODD) symptoms and teacher report of engagement in physical and relational aggression were collected. Models tested the unique association of EF abilities with physical and relational aggression and the indirect effect through the expression of ADHD or ODD behaviors; child gender was also tested as a moderator. EF impairment was uniquely associated with physical aggression, but better EF ability was associated with relational aggression. For boys, poor EF also was indirectly associated with greater physical aggression through the expression of ADHD behaviors. However, ADHD symptoms were unrelated to relational aggression. ODD symptoms also predicted physical aggression for boys but relational aggression for girls. Results suggest that there are multiple and distinct factors associated with engagement in physical

and relational aggression and that better EF may actually promote relational aggression. Established models of physical aggression should not be assumed to map on to explanations of relational aggression

.....

J Abnorm Child Psychol. 2017 Jul;45:841-55.

PARENTING AS A MECHANISM OF CHANGE IN PSYCHOSOCIAL TREATMENT FOR YOUTH WITH ADHD, PREDOMINANTLY INATTENTIVE PRESENTATION.

#### Haack LM, Villodas M, McBurnett K, et al.

We investigated whether parenting and child behavior improve following psychosocial treatment for Attention-Deficit/Hyperactivity Disorder, Predominantly Inattentive Presentation (ADHD-I) and whether parenting improvements mediate child outcomes. We analyzed data from a randomized clinical trial investigating the efficacy of a multicomponent psychosocial intervention (Child Life and Attention Skills, CLAS, n = 74) in comparison to Parent-Focused Treatment (PFT, n = 74) and treatment as usual (TAU, n = 51) for youth with ADHD-I (average child age = 8.6 years, range 7-11 years, 58 % boys). Child and parent/family functioning were assessed prior to treatment, immediately following treatment, and at follow-up into the subsequent school year using parent and teacher reports of inattention, organization, social skills, academic competency (teachers only), parenting daily hassles, and positive and negative parenting behaviors (parents only). Both treatment groups improved on negative parenting and home impairment, but only CLAS families also improved on positive parenting as well as academic impairment. Improvements in positive and negative parenting mediated treatment effects on child impairment independent of improvements in child inattention, implicating parenting as an important mechanism of change in psychosocial treatment for ADHD-I. Further, whereas parent-focused training produces improvements in negative parenting and impairment at home for children with ADHD-I, a multicomponent approach (incorporating child skills training and teacher consultation) more consistently produces improvements at school and in positive parenting, which may contribute to improvements in social skills into the next school year

.....

J Abnorm Child Psychol. 2017 Jul;45:1025-37.

PSYCHOEDUCATIONAL PSYCHOTHERAPY AND OMEGA-3 SUPPLEMENTATION IMPROVE CO-OCCURRING BEHAVIORAL PROBLEMS IN YOUTH WITH DEPRESSION: RESULTS FROM A PILOT RCT.

#### Young AS, Arnold LE, Wolfson HL, et al.

This pilot randomized controlled trial (RCT) investigated benefits of omega-3 fatty acid supplementation and Individual-Family Psychoeducational Psychotherapy (PEP; a family-focused, cognitive-behavioral therapy) for behavior problems among youth with depression. Participants aged 7-14 with DSM-IV-TR depressive disorders (N = 72; 56.9 % male) were randomized to 1 of 4 treatment conditions: PEP + omega-3, PEP monotherapy (with pill placebo), omega-3 monotherapy, or placebo (without active intervention). At screen, baseline, and 2, 4, 6, 9, and 12 weeks post-baseline, parents completed the SNAP-IV, which assesses attention-deficit/hyperactivity disorder symptoms, oppositional defiant disorder symptoms, and overall behavior problems. At screen, baseline (randomization), 6 and 12 weeks, parents completed the Eyberg Child Behavior Inventory (ECBI), which includes Intensity and Problem scales for child behavior problems. Youth who had a completed SNAP-IV or ECBI for at least two assessments during treatment (n = 48 and 38, respectively) were included in analyses of the respective outcome. ClinicalTrials.gov.:NCT01341925. Linear mixed effects models indicated a significant effect of combined PEP + omega-3 on SNAP-IV Total (p = 0.022, d = 0.80) and Hyperactivity/Impulsivity trajectories (p = 0.008, d = 0.80), such that youth in the combined group saw greater behavioral improvement than those receiving only placebo. Similarly, youth in combined treatment had more favorable ECBI Intensity trajectories than youth who received no active treatment (p = 0.012, d = 1.07). Results from this pilot RCT suggest that combined PEP + omega-3 is a promising treatment for co-occurring behavior symptoms in youth with depression

J Am Acad Child Adolesc Psychiatry. 2017 Jul;56:556-69.

CHILDHOOD PSYCHIATRIC DISORDERS AS RISK FACTOR FOR SUBSEQUENT SUBSTANCE ABUSE: A META-ANALYSIS.

Groenman AP, Janssen TWP, Oosterlaan J.

**OBJECTIVE**: To assess the prospective risk of developing substance-related disorders after childhood mental health disorders (i.e., attention-deficit/hyperactivity disorder [ADHD], oppositional defiant disorder [ODD] or conduct disorder [CD], anxiety disorder, and depression) using meta-analysis.

**METHOD**: PubMed, Embase, and PsycInfo were searched for relevant longitudinal studies that described childhood (<18 years old) ADHD, ODD or CD, anxiety, or depression in relation to later alcohol-, nicotine-, or drug-related disorders or substance use disorders (SUDs) published in peer-reviewed journals in the English language from 1986 to May 2016. Two researchers conducted all review stages. Meta-analysis of Observational Studies in Epidemiology (MOOSE) guidelines were followed.

**RESULTS**: Thirty-seven studies including more than 762,187 participants were identified for quantitative analyses. These studies included 22,029 participants with ADHD, 434 participants with ODD or CD, 1,433 participants with anxiety disorder, and 2,451 participants with depression. Ninety-seven effects sizes were extracted for analyses. Meta-analysis showed a significantly increased risk for addiction in ADHD (n = 23, odds ratio [OR] 2.27, 95% CI 1.98-3.67; OR alcohol 2.15, 95% CI 1.56-2.97; OR drugs 1.52, 95% CI 1.52-5.27; OR nicotine 2.52, 95% CI 2.01-3.15; OR SUDs 2.61, 95% CI 1.77-3.84), ODD or CD (n = 8, OR 3.18, 95% CI 1.97-5.80; OR alcohol 1.73, 95% CI 1.51-2.00; OR drugs 4.24, 95% CI 1.3.21.5.59; OR nicotine 4.22, 95% CI 3.21-5.55; OR SUDs 4.86, 95% CI 3.09-7.56), and depression (n = 13, OR 2.03, 95% CI 1.47-2.81; OR alcohol 1.10, 95% CI 1.02-1.19; OR nicotine 2.56, 95% CI 1.89-3.48; OR SUDs 2.20, 95% CI 1.41-3.43), but not for anxiety disorders (n = 15, OR 1.34, 95% CI 0.90-1.55, not significant).

**CONCLUSION**: Childhood ADHD, ODD, CD, and depression increase the risk of developing substance-related disorders. Anxiety disorders do not seem to increase the risk for future substance-related disorders, although the findings are highly heterogeneous. These findings emphasize the need for early detection and intervention to prevent debilitating substance-related disorders in later life

.....

J Am Acad Child Adolesc Psychiatry. 2017 Jul;56:610-17.

**AUTISM SPECTRUM SYMPTOMS IN A TOURETTE'S DISORDER SAMPLE.** 

Darrow SM, Grados M, Sandor P, et al.

**OBJECTIVE**: Tourette's disorder (TD) and autism spectrum disorder (ASD) share clinical features and possibly an overlapping etiology. The aims of this study were to examine ASD symptom rates in participants with TD, and to characterize the relationships between ASD symptom patterns and TD, obsessive-compulsive disorder (OCD), and attention-deficit/hyperactivity disorder (ADHD).

**METHOD**: Participants with TD (n = 535) and their family members (n =234) recruited for genetic studies reported TD, OCD, and ADHD symptoms and completed the Social Responsiveness Scale Second Edition (SRS), which was used to characterize ASD symptoms.

**RESULTS**: SRS scores in participants with TD were similar to those observed in other clinical samples but lower than in ASD samples (mean SRS total raw score = 51; SD = 32.4). More children with TD met cut-off criteria for ASD (22.8%) than adults with TD (8.7%). The elevated rate in children was primarily due to high scores on the SRS Repetitive and Restricted Behaviors (RRB) subscale. Total SRS scores were correlated with TD (r = 0.27), OCD (r = 0.37), and ADHD (r = 0.44) and were higher among individuals with OCD symptom-based phenotypes than for those with tics alone.

**CONCLUSION**: Higher observed rates of ASD among children affected by TD may in part be due to difficulty in discriminating complex tics and OCD symptoms from ASD symptoms. Careful examination of ASD-specific symptom patterns (social communication vs. repetitive behaviors) is essential. Independent of ASD, the SRS may be a useful tool for identifying patients with TD with impairments in social communication that potentially place them at risk for bullying and other negative sequelae

J Am Psychiatr Nurses Assoc. 2017 Mar;23:90-112.

PARENT AND FAMILY PROCESSES RELATED TO ADHD MANAGEMENT IN ETHNICALLY DIVERSE YOUTH.

Paidipati CP, Brawner B, Eiraldi R, et al.

**BACKGROUND**: Previous research has shown major disparities in attention deficit hyperactivity disorder (ADHD) for diverse youth across America. We do not fully understand, however, how parent and family processes are related to the identification, care-seeking approaches, treatment preferences, and engagement with care systems and services for youth with ADHD.

**OBJECTIVES**: The present study aimed to explore parent and family processes related to the management of ADHD in racially and ethnically diverse youth.

**DESIGN**: This integrative review was structured with the methodology proposed by Whittemore and Knafl.

**RESULTS**: Three major electronic databases yielded a final sample of 32 articles (24 quantitative, 6 qualitative, and 2 mixed methods). Nine themes emerged within three overarching meta-themes.

**CONCLUSIONS**: Understanding the unique perspectives of families from diverse backgrounds is essential for clinicians, researchers, and policymakers, who are dedicated to understanding racial and ethnic perspectives and developing ecologically appropriate and family-based interventions for youth with ADHD

.....

J Atten Disord. 2017 Sep;21:887-97.

PARENT- AND TEACHER-REPORTED SYMPTOMS OF ADHD IN SCHOOL-AGED CHILDREN WITH ACTIVE EPILEPSY: A POPULATION-BASED STUDY.

Reilly C, Atkinson P, Das KB, et al.

**OBJECTIVE**: Provide data on the distribution of parent- and teacher-reported symptoms of ADHD in childhood epilepsy and describe coexisting cognitive and behavioral disorders in children with both epilepsy and ADHD.

**METHOD**: Eighty-five (74% of those eligible) children (5-15 years) in a population-based sample with active epilepsy underwent psychological assessment. The ADHD Rating Scale-IV (ADHD-RS-IV) scale was completed by parents (n = 69) and teachers (n = 67) of participating children with an IQ > 34. ADHD was diagnosed with respect to Diagnostic and Statistical Manual of Mental Disorders (4th ed., text rev.).

**RESULTS**: Parents reported significantly more symptoms of ADHD than teachers (p < .001). Symptoms of inattention were more commonly reported than symptoms of hyperactivity-impulsivity (p < .001). Neurobehavioral comorbidity was similar in those with ADHD and non-ADHD with the exception of oppositional defiant disorder (ODD) and developmental coordination disorder (DCD), which were more common in those with both epilepsy and ADHD.

**CONCLUSION**: Symptoms of ADHD are very common in childhood epilepsy but prevalence is influenced by informant

.....

J Atten Disord, 2017 Sep:21:938-43.

MASCULINIZATION IN PARENTS OF OFFSPRING WITH AUTISM SPECTRUM DISORDERS COULD BE INVOLVED IN COMORBID ADHD SYMPTOMS.

Romero-Martinez A, Polderman TJC, Gonzalez-Bono E, et al.

**OBJECTIVE**: People with autism spectrum disorders (ASD) often have comorbid ADHD symptoms. ASD and ADHD are both associated with high intrauterine testosterone (T) levels. This study aims to investigate whether masculinization predicts inattention symptoms in parents, and in their ASD-affected offspring.

**METHOD**: The sample consisted of 32 parents with ASD-affected children (13 male, 19 female) and 32 offspring individuals (28 male, 4 female). Masculinization of parents was measured by 2D:4D finger ratio, and current T levels. Inattention in both parents and in their offspring was measured with behavior questionnaires.

**RESULTS**: The results indicated that masculinized 2D:4D explains inattentive ADHD symptoms in ASD parents and in their offspring. These predictions are mediated by T and inattention symptoms of ASD parents, respectively.

**CONCLUSION**: These findings suggest the existence of a masculinized endophenotype in ASD parents, which may be characterized by high attentional sensitivity to T effects

.....

J Atten Disord. 2017 Sep;21:921-28.

STRUCTURAL VALIDITY OF THE WISC-IV FOR STUDENTS WITH ADHD.

Styck KM, Watkins MW.

**OBJECTIVE**: To evaluate the structural validity of the Wechsler Intelligence Scale for Children-Fourth Edition (WISC-IV).

**METHOD**: Confirmatory factor analyses were applied to a sample of 233 students diagnosed with ADHD by school multidisciplinary evaluation teams to evaluate the relative fit of the following competing models: (a) one factor, (b) two oblique verbal and nonverbal factors, (c) three oblique verbal, perceptual, and combined working memory/processing speed factors, (d) four oblique verbal, perceptual, working memory, and processing speed factors, (e) a higher-order model with four first-order factors, and (f) a bifactor model with four domain-specific factors.

**RESULTS**: A higher-order four-factor model fit the data best, which was composed of a general intelligence factor and four domain-specific factors that matched the four factors specified in the WISC-IV technical and interpretive manual. Moreover, the general intelligence factor explained more than two times the total variance contributed by all four domain-specific factors combined.

**CONCLUSIONS**: Results substantiate previous research on the WISC-IV, indicating that the general intelligence factor contributes the most reliable information. Consequently, it is recommended that interpretation of the WISC-IV remain at the Full-Scale IQ score level

.....

J Atten Disord. 2017 Sep;21:913-20.

CULTURALLY APPROPRIATE ASSESSMENT OF FUNCTIONAL IMPAIRMENT IN DIVERSE CHILDREN: VALIDATION OF THE ADHD-FX Scale With an At-Risk Community Sample.

Haack LM. Gerdes AC.

**OBJECTIVE**: In an effort to reduce disparities in ADHD diagnoses and treatment across cultures, the current study sought to establish initial psychometric and cultural properties of the ADHD-FX: a culturally sensitive assessment measure of functional impairment related to ADHD for diverse families.

**METHOD**: Fifty-four Latino parents (44 mothers and 10 fathers) of school-aged children completed the ADHD-FX, as well as several other measures assessing child behavior and parent acculturation.

**RESULTS**: The ADHD-FX demonstrated adequate reliability (as demonstrated by internal consistency and test-retest reliability), psychometric construct validity (as demonstrated by associations with theoretically related measures), and cultural validity (as demonstrated by or lack of associations with acculturation measures).

**CONCLUSION**: Initial psychometric and cultural properties suggest that the ADHD-FX is a reliable, valid, and culturally appropriate measure to assess functional impairment related to ADHD (i.e., difficulties with academic achievement, social competence, and familial relationships) in an at-risk, school-aged population

.....

J Atten Disord. 2017 Sep;21:898-903.

A PRELIMINARY EXAMINATION OF AEROBIC EXERCISE EFFECTS ON RESTING EEG IN CHILDREN WITH ADHD.

Huang CJ, Huang CW, Tsai YJ, et al.

**OBJECTIVE**: This study attempted to determine whether the effects of physical exercise were reflected in the resting electroencephalographic (EEG) pattern of ADHD children.

**METHOD**: Thirty-two ADHD children were assigned to either an exercise group or a control group. The exercise group participated in a water aerobics program for 8 weeks, whereas no intervention was administered to the control group. Resting EEGs were recorded under open-eyes condition before and after

the intervention. Data from eligible participants, 15 from the exercise group (11 boys and 4 girls, 7.93 +/- 1.02 years) and 14 from the control group (14 boys, 8.27 +/- 1.04 years), were further analyzed.

**RESULTS**: While controlling for the baseline resting EEG, separate ANCOVAs indicated that the exercise group showed smaller theta/alpha ratios over the frontal and central brain sites after the intervention compared with the control group.

**CONCLUSION**: This finding suggests that aerobic exercise may enhance the cognitive functions of children with ADHD, as reflected in resting EEG

.....

J Atten Disord. 2017 Sep;21:904-12.

DIFFERENT RISK FACTORS BETWEEN DISRUPTIVE BEHAVIOR DISORDERS AND ADHD IN NORTHERN FINLAND BIRTH COHORT 1986.

Nordstrom T, Hurtig T, Rodriguez A, et al.

**OBJECTIVE**: To examine different risk factors between disruptive behavior disorders (DBD) and ADHD or combined DBD and ADHD.

**METHOD**: The study population was derived from the Northern Finland Birth Cohort 1986. Psychiatric diagnoses were defined from the Schedule for Affective Disorders and Schizophrenia for School-Age Children-Present and Lifetime Version (K-SADS-PL) interview. The study sample was divided into four groups-people with DBD (n = 44), with ADHD (n = 91), with both (n = 72), and without either (n = 250)-to evaluate the different risk factors behind these disorders.

**RESULTS**: After adjusting with possible confounding factors, female gender and paternal admittance to inpatient psychiatric care increased the odds that an adolescent was having DBD. Childhood hyperactivity symptoms increased the odds of having ADHD and childhood hyperactivity symptoms and scholastic impairment increased the odds of having both disorders.

**CONCLUSION**: Our study indicates DBD and ADHD have clearly different risk factors, and the impact of the paternal factors on DBD should be noted more than has been before

.....

J Atten Disord. 2017 Sep;21:929-37.

EXAMINATION OF THE EFFECTS OF INTELLIGENCE ON THE TEST OF VARIABLES OF ATTENTION FOR ELEMENTARY STUDENTS.

Hurford DP, Fender AC, Boux JL, et al.

**OBJECTIVE**: To examine the performance differences on the Test of Variables of Attention (TOVA) among different IQ level groups.

**METHOD**: The present study examined the results of the TOVA with 138 elementary students aged 6 to 10 years who were assigned to one of four different groups based on their scores from the Wechsler Nonverbal Scale of Ability (WNV; low average: IQ < 90, average: IQ between 90 and 109, high average: IQ between 110 and 119, superior: IQ between 120 and 129, and very superior: IQ > 129). The latter two groups were combined.

**RESULTS**: On all TOVA measures (response time, response time variability, errors of omission and commission, and ADHD scores), intellectual functioning significantly influenced performance.

**CONCLUSION**: The results of the present study indicate that performance on the TOVA was affected by intellectual functioning

Newsletter – ADHD marzo 2018

J Atten Disord. 2017 Sep;21:956-68.

WORKING MEMORY TRAINING IN ADHD: CONTROLLING FOR ENGAGEMENT, MOTIVATION, AND EXPECTANCY OF IMPROVEMENT (PILOT STUDY).

Mawjee K, Woltering S, Lai N, et al.

**OBJECTIVE**: The aim of this study was to evaluate whether a shortened-length session of CogMed Working Memory Training (CWMT) would be a suitable active control group and evaluate study protocol to aid in design refinements for a larger randomized controlled trial (RCT).

**METHOD**: Thirty-eight post-secondary students diagnosed with ADHD were randomized into 25 sessions of standard (45 min/session) or shortened (15 min/session) CWMT, or into a waitlist control group.

**RESULTS**: There was no significant difference in completion rate or training index score between the standard- and shortened-length groups indicating that both groups showed improvement and put forth good effort during training.

**CONCLUSION**: Preliminary findings suggest that shorter training sessions may induce similar levels of engagement, motivation, and expectancy of improvement in participants. We conclude that a larger scale RCT that utilizes shortened-length training as an active control group is warranted, but that a few modifications to the study protocol will be required

.....

J Child Adolesc Ment Health. 2017 May;29:51-61.

SUBSTANCE USE IN ADOLESCENTS WITH MENTAL ILLNESS IN DURBAN, SOUTH AFRICA.

#### Taukoor B, Paruk S, Karim E, et al.

Comorbid substance use in adolescents with mental illness is often an indicator of poor treatment outcome. This study aims to determine the prevalence of, and associated risk factors for, substance use in adolescents with mental illness attending a mental health service. Data was collected from hospital records of 162 adolescents, using a structured data sheet, over a two-year period. Substance use was more significant in older adolescents and those with severe mental illness. Sixty-two (38.3%) adolescents used substances. Thirty-seven (38.1%) male adolescents reported substance use compared to 25 (38.5%) female adolescents. Alcohol was the most commonly used substance (n = 48; 29.6%), followed by cannabis (n = 32; 19.8%). There were significant direct associations between substance use and history of abuse or neglect, forensic history, educational setting, admission status, and the psychiatric diagnoses of schizophrenia, other psychotic disorders, and bipolar mood disorder. Inverse associations were found between substance use and adjustment disorders, attention deficit hyperactivity disorder, and intellectual disability. The results of this study indicate an urgent need for substance misuse programmes for at risk youth, and the introduction of dual diagnosis intervention programmes in this age group

.....

J Child Adolesc Psychopharmacol. 2017 Jun;27:445-50.

FACTORS ASSOCIATED WITH MANAGEMENT OF TEEN AGGRESSION: CHILD PSYCHIATRIC CLINICAL DECISION MAKING.

Mann A, Li A, Radwan K, et al.

**OBJECTIVE**: This study explores whether patient-specific and clinician-specific factors are associated with child psychiatrists' use of second generation antipsychotics (SGAs) in the management of aggression in children with attention-deficit/hyperactivity disorder (ADHD). The patient-specific factors included patient's race, caregiver status, and patient engagement in psychotherapy.

**METHODS**: Child psychiatrists attending an annual conference (n = 156) were asked to complete an anonymous questionnaire on clinical decision making. Each participant was randomized to one of eight vignettes on a physically aggressive male teenager with methylphenidate-responsive ADHD. Patient race, caregiving status, and patient engagement in psychotherapy were systematically varied. Respondents rated how likely they were to prescribe an SGA and whether they would adjust the patient's current medication.

**RESULTS**: Seventy-five percent of participants (n = 117) were uncomfortable with adding an SGA, and 61% (n = 95) were likely to make medication adjustments to the current stimulant. None of the patient-specific

factors were related to management recommendations. However, inpatient psychiatrists compared with non-inpatient psychiatrists reported a higher likelihood of using antipsychotics (OR = 2.40, 95% CI [1.181, 4.879], p = 0.016). Midwestern psychiatrists compared with those from other regions also reported a higher likelihood of using antipsychotics (OR = 3.07, 95% CI [1.376, 6.857], p = 0.005). Academic psychiatrists compared with nonacademics were less likely to endorse making adjustments to the current medication regimen (OR = 0.49, 95% CI [0.860, 0.274], p = 0.013).

**CONCLUSIONS**: When presented with a hypothetical case, the vast majority of child psychiatrists surveyed advised that additional information was needed before adding an SGA. Many felt the need for more psychosocial information and greater clarity of possible comorbid diagnoses

.....

J Child Adolesc Psychopharmacol. 2017 May;27:320-31.

AN EVALUATION APPROACH FOR THE PERFORMANCE OF DOSING REGIMENS IN ATTENTION-DEFICIT/HYPERACTIVITY DISORDER TREATMENT.

## Bonnefois G, Robaey P, Barriere O, et al.

**OBJECTIVE**: Stimulant medications, with methylphenidate as the main agent, are the most prescribed for the treatment of attention-deficit/hyperactivity disorder. Nevertheless, real challenges still remain for clinicians concerned with adaptation of the therapeutic regimens, in terms of doses and timing, to children's daily activities. The aim of this study was to optimize short-acting methylphenidate regimens according to specific children's needs by evaluating the performance of a particular regimen through a web-based application.

**METHODS**: In this article, accounting for day-to-day children's activities and using up-to-date pharmacokinetic knowledge of methylphenidate, we propose a computational approach for the identification of the most suitable dosing regimens of immediate-release formulations of methylphenidate based on constraints on drug concentration and time frame of activities, defined through therapeutic boxes. To assess the performance of these regimens, time- and concentration-based therapeutic indicators, as well as a roller coaster effect, are proposed.

**RESULTS**: A web-based interface that can serve as an educational tool for clinicians and patients has been developed based on the proposed approach for the evaluation of dosing regimens. Comparison of those optimal regimens identified by our method with the well-accepted regimens defined in the NIMH Collaborative Multisite Multimodal Treatment study of Children with attention-deficit/hyperactivity disorder indicates that there is still room for improvement in the current practice especially for the last dose administration to avoid side effects such as sleep disturbance.

**CONCLUSION**: The developed approach and its associated web-based interface provide an efficient way to evaluate and adapt the methylphenidate regimens to children's daily activities. In addition, this approach could be used as proof of concept to further implement combination of short- and long-acting methylphenidate

.....

J Child Adolesc Psychopharmacol. 2017 Jun;27:422-28.

ATTITUDES TOWARD STIMULANT TREATMENT OF OFFSPRING OF ADULT PATIENTS WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.

#### Canela C, Buadze A, Dube A, et al.

**AIM**: The objective of this study was to investigate how adult patients with attention-deficit/hyperactivity disorder viewed the testing and use of stimulants in their children.

**METHODS**: Using a qualitative approach, we interviewed 32 outpatients from a special care unit of a university hospital.

**RESULTS**: Emerging themes centered around concerns about the right age to test children and opinions about stimulant treatment ranging from unreserved agreement to reluctance, as well as the need for a shared decision with the child.

**CONCLUSIONS**: Our results suggest that better psychoeducational programs are needed, especially for adults with attention-deficit/hyperactivity disorder, in which long-term consequences of the disorder, areas of impairment, and possible treatment effects in their children are explained and concerns about unknown side effects and the right time to test and treat are addressed

.....

J Child Neurol. 2017 Jun:32:663-70.

SECONDARY CONDITIONS AMONG MALES WITH DUCHENNE OR BECKER MUSCULAR DYSTROPHY.

#### Latimer R, Street N, Conway KC, et al.

Duchenne and Becker muscular dystrophy are X-linked neuromuscular disorders characterized by progressive muscle degeneration. Despite the involvement of multiple systems, secondary conditions among affected males have not been comprehensively described. Two hundred nine caregivers of affected males (aged 3-31 years) identified by the Muscular Dystrophy Surveillance, Tracking, and Research Network completed a mailed survey that included questions about secondary conditions impacting multiple body functions. The 5 most commonly reported conditions in males with Duchenne were cognitive deficits (38.4%), constipation (31.7%), anxiety (29.3%), depression (27.4%), and obesity (19.5%). Higher frequencies of anxiety, depression, and kidney stones were found among nonambulatory males compared to ambulatory males. Attention-deficit hyperactivity disorder (ADHD) was more common in ambulatory than nonambulatory males. These data support clinical care recommendations for monitoring of patients with Duchenne or Becker muscular dystrophy by a multidisciplinary team to prevent and treat conditions that may be secondary to the diagnosis

.....

J Child Psychol Psychiatry. 2017 Jun;58:663-78.

YOUNG ADULT OUTCOMES IN THE FOLLOW-UP OF THE MULTIMODAL TREATMENT STUDY OF ATTENTION-DEFICIT/HYPERACTIVITY DISORDER: SYMPTOM PERSISTENCE, SOURCE DISCREPANCY, AND HEIGHT SUPPRESSION.

# Swanson JM, Arnold LE, Molina BSG, et al.

**BACKGROUND**: The Multimodal Treatment Study (MTA) began as a 14-month randomized clinical trial of behavioral and pharmacological treatments of 579 children (7-10 years of age) diagnosed with attention-deficit/hyperactivity disorder (ADHD)-combined type. It transitioned into an observational long-term follow-up of 515 cases consented for continuation and 289 classmates (258 without ADHD) added as a local normative comparison group (LNCG), with assessments 2-16 years after baseline.

**METHODS**: Primary (symptom severity) and secondary (adult height) outcomes in adulthood were specified. Treatment was monitored to age 18, and naturalistic subgroups were formed based on three patterns of long-term use of stimulant medication (Consistent, Inconsistent, and Negligible). For the follow-up, hypothesis-generating analyses were performed on outcomes in early adulthood (at 25 years of age). Planned comparisons were used to estimate ADHD-LNCG differences reflecting persistence of symptoms and naturalistic subgroup differences reflecting benefit (symptom reduction) and cost (height suppression) associated with extended use of medication.

**RESULTS**: For ratings of symptom severity, the ADHD-LNCG comparison was statistically significant for the parent/self-report average (0.51 +/- 0.04, p < .0001, d = 1.11), documenting symptom persistence, and for the parent/self-report difference (0.21 +/- 0.04, p < .0001, d = .60), documenting source discrepancy, but the comparisons of naturalistic subgroups reflecting medication effects were not significant. For adult height, the ADHD group was 1.29 +/- 0.55 cm shorter than the LNCG (p < .01, d = .21), and the comparisons of the naturalistic subgroups were significant: the treated group with the Consistent or Inconsistent pattern was 2.55 +/- 0.73 cm shorter than the subgroup with the Negligible pattern (p < .0005, d = .42), and within the treated group, the subgroup with the Consistent pattern was 2.36 +/- 1.13 cm shorter than the subgroup with the Inconsistent pattern (p < .04, d = .38).

**CONCLUSIONS**: In the MTA follow-up into adulthood, the ADHD group showed symptom persistence compared to local norms from the LNCG. Within naturalistic subgroups of ADHD cases, extended use of medication was associated with suppression of adult height but not with reduction of symptom severity

.....

J Child Psychol Psychiatry. 2017 Jun;58:719-27.

EXPLAINING THE SEX DIFFERENCE IN DYSLEXIA.

Arnett AB, Pennington BF, Peterson RL, et al.

**BACKGROUND**: Males are diagnosed with dyslexia more frequently than females, even in epidemiological samples. This may be explained by greater variance in males' reading performance.

**METHODS**: We expand on previous research by rigorously testing the variance difference theory, and testing for mediation of the sex difference by cognitive correlates. We developed an analytic framework that can be applied to group differences in any psychiatric disorder.

**RESULTS**: Males' overrepresentation in the low performance tail of the reading distribution was accounted for by mean and variance differences across sex. There was no sex difference at the high performance tail. Processing speed (PS) and inhibitory control partially mediated the sex difference. Verbal reasoning emerged as a strength in males.

**CONCLUSIONS**: Our results complement a previous finding that PS partially mediates the sex difference in symptoms of attention deficit/hyperactivity disorder (ADHD), and helps explain the sex difference in both dyslexia and ADHD and their comorbidity

.....

J Child Psychol Psychiatry. 2017 Jun;58:691-701.

MALTREATMENT-ASSOCIATED NEURODEVELOPMENTAL DISORDERS: A CO-TWIN CONTROL ANALYSIS.

Dinkler L, Lundstrom S, Gajwani R, et al.

**BACKGROUND**: Childhood maltreatment (CM) is strongly associated with psychiatric disorders in childhood and adulthood. Previous findings suggest that the association between CM and psychiatric disorders is partly causal and partly due to familial confounding, but few studies have investigated the mechanisms behind the association between CM and neurodevelopmental disorders (NDDs). Our objective was to determine whether maltreated children have an elevated number of NDDs and whether CM is a risk factor for an increased NDD 'load' and increased NDD symptoms when controlling for familial effects.

**METHODS**: We used a cross-sectional sample from a population-representative Swedish twin study, comprising 8,192 nine-year-old twins born in Sweden between 1997 and 2005. CM was defined as parent-reported exposure to emotional abuse/neglect, physical neglect, physical abuse, and/or sexual abuse. Four NDDs were measured with the Autism-Tics, AD/HD, and other comorbidities inventory.

**RESULTS**: Maltreated children had a greater mean number of NDDs than nonmaltreated children. In a cotwin control design, CM-discordant monozygotic twins did not differ significantly for their number of NDDs, suggesting that CM is not associated with an increased load of NDDs when genetic and shared environmental factors are taken into account. However, CM was associated with a small increase in symptoms of attention-deficit/hyperactivity disorder and autism spectrum disorder in CM-discordant MZ twins, although most of the covariance of CM with NDD symptoms was explained by common genetic effects. **CONCLUSIONS**: Maltreated children are at higher risk of having multiple NDDs. Our findings are, however, not consistent with the notion that CM causes the increased NDD load in maltreated children. Maltreated children should receive a full neurodevelopmental assessment, and clinicians should be aware that children with multiple NDDs are at higher risk of maltreatment

J Child Psychol Psychiatry. 2017 Jun;58:711-18.

SHARED FAMILIAL RISK FACTORS BETWEEN ATTENTION-DEFICIT/HYPERACTIVITY DISORDER AND OVERWEIGHT/OBESITY - A POPULATION-BASED FAMILIAL COAGGREGATION STUDY IN SWEDEN.

Chen Q, Kuja-Halkola R, Sjolander A, et al.

**BACKGROUND**: Despite meta-analytic evidence for the association between attention-deficit/hyperactivity disorder (ADHD) and overweight/obesity, the mechanisms underlying the association are yet to be fully understood.

**METHODS**: By linking multiple Swedish national and regional registers, we identified 472,735 index males born during 1973-1992, with information on body weight and height directly measured before they were conscripted for military service. We further identified 523,237 full siblings born during 1973-2002 for the index males. All individuals were followed up from their third birthday to December 31, 2009 for ADHD diagnosis. Logistic regression models were used to estimate the association between overweight/obesity in index males and ADHD in their full siblings.

**RESULTS**: Siblings of index males with overweight/obesity had increased risk for ADHD (overweight: OR = 1.14, 95% CI = 1.05-1.24; obesity: OR = 1.42, 95% CI = 1.24-1.63), compared with siblings of index males with normal weight. The results were adjusted for birth year of the index male and sex of the sibling. After further adjustment for ADHD status of the index male, the familial coaggregation remained significant (overweight: OR = 1.13, 95% CI = 1.04-1.22; obesity: OR = 1.38, 95% CI = 1.21-1.57). The results were similar across sex of the siblings.

**CONCLUSIONS**: Attention-deficit/hyperactivity disorder and overweight/obesity share familial risk factors, which are not limited to those causing overweight/obesity through the mediation of ADHD. Future research aiming at identifying family-wide environmental risk factors as well as common pleiotropic genetic variants contributing to both traits is warranted

.....

J Child Psychol Psychiatry. 2017 Jul;58:798-809.

SLC2A3 SINGLE-NUCLEOTIDE POLYMORPHISM AND DUPLICATION INFLUENCE COGNITIVE PROCESSING AND POPULATION-SPECIFIC RISK FOR ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.

Merker S, Reif A, Ziegler GC, et al.

**BACKGROUND**: Attention-deficit/hyperactivity disorder (ADHD) is a common, highly heritable neurodevelopmental disorder with profound cognitive, behavioral, and psychosocial impairments with persistence across the life cycle. Our initial genome-wide screening approach for copy number variants (CNVs) in ADHD implicated a duplication of SLC2A3, encoding glucose transporter-3 (GLUT3). GLUT3 plays a critical role in cerebral glucose metabolism, providing energy for the activity of neurons, which, in turn, moderates the excitatory-inhibitory balance impacting both brain development and activity-dependent neural plasticity. We therefore aimed to provide additional genetic and functional evidence for GLUT3 dysfunction in ADHD.

**METHODS**: Case-control association analyses of SLC2A3 single-nucleotide polymorphisms (SNPs) and CNVs were conducted in several European cohorts of patients with childhood and adult ADHD (SNP, n=1,886 vs. 1,988; CNV, n=1,692 vs. 1,721). These studies were complemented by SLC2A3 expression analyses in peripheral cells, functional EEG recordings during neurocognitive tasks, and ratings of food energy content.

**RESULTS**: Meta-analysis of all cohorts detected an association of SNP rs12842 with ADHD. While CNV analysis detected a population-specific enrichment of SLC2A3 duplications only in German ADHD patients, the CNV + rs12842 haplotype influenced ADHD risk in both the German and Spanish cohorts. Duplication carriers displayed elevated SLC2A3 mRNA expression in peripheral blood cells and altered event-related potentials reflecting deficits in working memory and cognitive response control, both endophenotypic traits of ADHD, and an underestimation of energy units of high-caloric food.

**CONCLUSIONS**: Taken together, our results indicate that both common and rare SLC2A3 variation impacting regulation of neuronal glucose utilization and energy homeostasis may result in neurocognitive deficits known to contribute to ADHD risk

J Child Psychol Psychiatry. 2017 Jul;58:810-18.

STRUCTURAL AND FUNCTIONAL CONNECTIVITY IN CHILDREN AND ADOLESCENTS WITH AND WITHOUT ATTENTION DEFICIT/HYPERACTIVITY DISORDER.

Bos DJ, Oranje B, Achterberg M, et al.

**BACKGROUND**: Attention deficit/hyperactivity disorder (ADHD) has frequently been associated with changes in resting-state functional connectivity, and decreased white matter (WM) integrity. In the current study, we investigated functional connectivity within Default Mode and frontal control resting-state networks (RSNs) in children with and without ADHD. We hypothesized the RSNs of interest would show a pattern of impaired functional integration and segregation and corresponding changes in WM structure.

**METHODS**: Resting-state fMRI and diffusion-weighted imaging data were acquired from 35 participants with ADHD and 36 matched typically developing peers, aged 6 through 18 years. Functional connectivity was assessed using independent component analysis. Network topology and WM connectivity were further investigated using graph theoretical measures and tract-based spatial statistics (TBSS).

**RESULTS**: Resting-state fMRI analyses showed increased functional connectivity in right inferior frontal gyrus (IFG), and bilateral medial prefrontal cortex (mPFC) within the Default Mode and frontal control networks. Furthermore, a more diffuse spatial pattern of functional connectivity was found in children with ADHD. We found no group differences in structural connectivity as assessed with TBSS or graph theoretical measures.

**CONCLUSIONS**: Resting-state networks show a more diffuse pattern of connectivity in children with ADHD. The increases in functional connectivity in right IFG and bilateral mPFC in children with ADHD may reflect reduced or delayed functional segregation of prefrontal brain regions. As these functional changes were not accompanied by changes in WM, they may precede the development of the frequently reported changes in WM structure

.....

J Dev Behav Pediatr. 2017 Jun;38:349-51.

AUDITORY PROCESSING DISORDER: WHAT DOES IT MEAN AND WHAT CAN BE DONE?

Bartlett K, Kelley E, Purdy J, et al.

CASE: Julian, an 11-year-old boy in the sixth grade with a compliant disposition and a positive attitude, has had a significant decline in his academic performance over the last 2 years. He spends much of his time in the nurse's office with headaches and fatigue. He reports that he cannot concentrate or follow along in class. Vision and hearing screenings were normal. Julian's teachers report that although he has no behavior problem, he is inattentive and does not put forth the effort she feels he is capable of giving. He does not seem to be listening, and he is distracted by everyone around him. He often claims that he did not hear or understand the things that teachers explained several times. When teachers talk to him directly, he starts an assignment and usually finishes his work on time. Teachers observe that he has "attention-deficit hyperactive disorder (ADHD) like tendencies." A recent psychoeducational evaluation qualified Julian for special education services under specific learning disability in the area of auditory processing. An individual education plan will be developed within the next 2 weeks. Key indicators used to make this determination included the following: average standard scores on nonverbal tests of cognitive development, a belowaverage score in overall auditory processing (with particularly low scores in auditory reasoning and auditory memory), average scores in the areas of general memory and attention/concentration, and below-average composite scores in reading and written expression. Following a review of the assessment report, Julian's parents remain concerned about the possibility of ADHD. Prior to the special education assessment, the school provided the Vanderbilt Assessment Scales for Julian's parents to share with his doctors; it revealed elevated scores in ADHD symptoms (predominantly inattentive subtype). Julian's parents would like to learn about options for treatment that might improve his attention

J Epidemiol Community Health. 2017 Jul;71:648-54.

ASSOCIATION BETWEEN INCOME TRAJECTORIES IN CHILDHOOD AND PSYCHIATRIC DISORDER: A SWEDISH POPULATION-BASED STUDY.

Bjorkenstam E, Cheng S, Burstrom B, et al.

**BACKGROUND**: Childhood family income variation is an understudied aspect of households' economic context that may have distinct consequences for children. We identified trajectories of childhood family income over a 12-year period, and examined associations between these trajectories and later psychiatric disorders, among individuals born in Sweden between 1987 and 1991 (n=534 294).

**METHODS**: We used annual income data between the ages of 3-14 years and identified 5 trajectories (2 high-income upward, 1 downward and 2 low-income upward trajectories). Psychiatric disorders in the follow-up period after age 15 were defined from International Classification of Disease (ICD)-codes in a nationwide patient register. Multiadjusted risks for all psychiatric disorders, as well as for specific psychiatric diagnoses, were calculated as HRs with 95% CIs.

**RESULTS**: Of the 5 identified income trajectories, the constant low and the downward trajectories were particularly associated with later psychiatric disorder. Children with these trajectories had increased risks for psychiatric disorder, including mood, anxiety, psychotic disorders and attention deficit/hyperactivity disorder. The association remained, even after adjusting for important variables including parental psychiatric disorder. In contrast, the relationship was reversed for eating disorders, for which children in higher income trajectories had elevated risks.

**CONCLUSIONS**: Findings show that children growing up in a household characterised by low or decreasing family income have an increased risk for psychiatric disorder. Continued work is needed to reduce socioeconomic inequalities in psychiatric disorders. Policies and interventions for psychiatric disorders should consider the socioeconomic background of the family as an important risk or protective factor

.....

J Forensic Sci. 2017 Mar:62:528-30.

SELF-STRANGULATION THROUGH A SPHYGMOMANOMETER: AN UNCOMMON SUICIDE.

#### Lo PS, Tacchella T, Fossati F, et al.

Suicide by asphyxia is quite a common event in forensic practice and may be implemented in different ways. The authors report a unique case of a 16-year-old youth who committed suicide by means of a standard mercury sphygmomanometer. This manner of suicide has never been described in the literature reviewed. A complete forensic investigation led to the conclusion that the cause of death was mechanical asphyxia, ascribed to self-strangulation by means of an atypical item. The victim suffered from attention-deficit/hyperactivity disorder (ADHD) syndrome and was assisted by support teachers. He had a solitary and depressive personality. The exceptional nature of this case suggests that sphygmomanometers may be regarded as possible means of self-strangulation. The case also highlights the importance of managing patients with psychiatric or cognitive disorders; indeed, particular caution is required to keep them away from objects that, although apparently harmless, can become lethal

.....

J Learn Disabil. 2017 Jul:50:408-21.

COGNITIVE PREDICTION OF READING, MATH, AND ATTENTION: SHARED AND UNIQUE INFLUENCES.

#### Peterson RL, Boada R, McGrath LM, et al.

The current study tested a multiple-cognitive predictor model of word reading, math ability, and attention in a community-based sample of twins ages 8 to 16 years (N=636). The objective was to identify cognitive predictors unique to each skill domain as well as cognitive predictors shared among skills that could help explain their overlap and thus help illuminate the basis for comorbidity of related disorders (reading disability, math disability, and attention deficit hyperactivity disorder). Results indicated that processing speed contributes to the overlap between reading and attention as well as math and attention, whereas verbal comprehension contributes to the overlap between reading and math. There was no evidence that executive functioning skills help account for covariation among these skill domains. Instead, specific executive functions

differentially related to certain outcomes (i.e., working memory to math and inhibition to attention). We explored whether the model varied in younger versus older children and found only minor differences. Results are interpreted within the context of the multiple deficit framework for neurodevelopmental disorders

.....

J Learn Disabil. 2017 Jul;50:434-49.

RELATIONSHIPS OF ATTENTION AND EXECUTIVE FUNCTIONS TO ORAL LANGUAGE, READING, AND WRITING SKILLS AND SYSTEMS IN MIDDLE CHILDHOOD AND EARLY ADOLESCENCE.

## Berninger V, Abbott R, Cook CR, et al.

Relationships between attention/executive functions and language learning were investigated in students in Grades 4 to 9 ( N = 88) with and without specific learning disabilities (SLDs) in multiword syntax in oral and written language (OWL LD), word reading and spelling (dyslexia), and subword letter writing (dysgraphia). Prior attention-deficit/hyperactivity disorder (ADHD) diagnosis was correlated only with impaired handwriting. Parental ratings of inattention, but not hyperactivity, correlated with measures of written language but not oral language. Sustaining switching attention correlated with writing the alphabet from memory in manuscript or by keyboard and fast copying of a sentence with all the letters of the alphabet. Multiple regressions based on a principal component for composites of multiple levels of language (subword, word, and syntax/text) showed that measures of attention and executive function involving language processing rather than ratings of attention and executive function not specifically related to language accounted for more variance and identified more unique predictors in the composite outcomes for oral language, reading, and writing systems. Inhibition related to focused attention uniquely predicted outcomes for the oral language system. Findings are discussed in reference to implications for assessing and teaching students who are still learning to pay attention to heard and written language and self-regulate their language learning during middle childhood and adolescence

.....

J Pediatr Health Care. 2016 Nov;30:e43-e48.

AN INTERVENTION TO PROMOTE SLEEP AND REDUCE ADHD SYMPTOMS.

Peppers KH, Eisbach S, Atkins S, et al.

**OBJECTIVE**: To determine the effect of a sleep hygiene education module and prescriptive sleep routine for children ages 5 through 11 years with attention deficit hyperactivity disorder (ADHD).

**METHODS**: The 20-week pilot project used a pre-/posttest design to assess sleep and ADHD symptoms. The Child Sleep Habits Questionnaire (CHSQ) and Vanderbilt Assessment Scale-Parent Form survey were provided to assess sleep and ADHD behaviors of participants at baseline and 6 weeks after implementation of the sleep hygiene routine. Fifty-three children participated in the project. Of these, 23 scored 42 or greater on the CHSQ, indicating a sleep disorder, and received the intervention.

**RESULTS**: The CHSQ and Vanderbilt scores indicated a significant improvement in sleep quality and reduction in ADHD symptoms after implementation of the sleep hygiene routine (CHSQ: p < .001, d = .928; Vanderbilt Questions 1-9: p < .001, d = .473; Vanderbilt Questions 10-18: p = .004; d = .329).

**CONCLUSION**: A provider-instructed sleep hygiene routine in children with ADHD improves sleep quality and reduces ADHD symptoms

J Psychiatr Res. 2017 Sep;92:124-31.

THE DIMENSIONAL STRUCTURE OF PSYCHOPATHOLOGY IN 22Q11.2 DELETION SYNDROME.

Niarchou M, Moore TM, Tang SX, et al.

**BACKGROUND**: 22q11.2 Deletion Syndrome (22q11.2DS) is one of the strongest known genetic risk factors for developing schizophrenia. Individuals with 22q11.2DS have high rates of neurodevelopmental disorders in childhood, while in adulthood approximately 25% develop schizophrenia. Similar to the general population, high rates of comorbidity are common in 22q11.2DS. Employing a dimensional approach where

Newsletter – ADHD marzo 2018

psychopathology is examined at the symptom-level as complementary to diagnostic categories in a population at such high genetic risk for schizophrenia can help gain a better understanding of how psychopathology is structured as well as its genetic underpinnings. This is the first study to examine the dimensional structure of a wide spectrum of psychopathology in the context of a homogeneous genetic etiology like 22q11.2DS.

**METHODS**: We evaluated 331 individuals with 22q11.2DS, mean age (SD) = 16.9(8.7); 51% males, who underwent prospective comprehensive phenotyping. We sought to replicate previous findings by examining a bi-factor model that derives a general factor of psychopathology in addition to more specific dimensions of psychopathology (i.e., internalizing, externalizing and thought disorder).

**RESULTS**: Psychopathology in 22q11.2DS was divided into one 'general psychopathology' factor and four specific dimensions (i.e., 'anxiety', 'mood', 'ADHD' and 'psychosis'). The 'psychosis' symptoms loaded strongly on the 'general psychopathology' factor.

**CONCLUSIONS**: The similarity of the symptom structure of psychopathology between 22q11.2DS and community and clinical populations without the deletion indicate that 22q11.2DS can provide a model to explore alternative approaches to our current nosology. Our findings add to a growing literature indicating the need to reorganize current diagnostic classification systems

.....

J Psychiatr Res. 2017 Jul;90:118-25.

COMPOSITE IMPULSIVITY-RELATED DOMAINS IN COLLEGE STUDENTS.

#### Khadka S, Stevens MC, Aslanzadeh F, et al.

Impulsivity is a complex, multidimensional construct with prior theoretically and empirically derived characterizations of impulsivity-related behaviors varying considerably among studies. We assessed college students (N = 440) longitudinally with five impulsivity-related self-reported assessments and two computerized behavioral measures. Using a combination of exploratory and confirmatory factor analysis (CFA), we derived then validated several composite impulsivity-related domains (CIRDs). These factors replicated, in large part, findings from a previous study conducted by our group in an independent sample that used a similar analytical approach. The four CIRDs derived in current study are: 'Impulsive action', 'Approach/Appetite Motivation', 'Impulsivity/Compulsivity' and 'Experience and thrill seeking/Fearlessness'. Subsequent psychometric analyses found these CIRDs were relatively stable over the two-year period. Moreover, multiple regression analysis found that CIRD profiles associated with clinical and behavioral characteristics including anxiety, depression, attention deficit hyperactivity disorder and substance use symptomology. Overall, our data suggest that empirically-derived CIRDs have potential for organizing previous impulsivity-related constructs into a more naturalistic framework where distinct constructs are often expressed together in the same individuals. This framework might facilitate future research of neuropsychiatric disorder risk and etiology

.....

J Psychosoc Nurs Ment Health Serv. 2016 Aug;54:29-34.

GENETIC AND ENVIRONMENTAL INFLUENCES ON THE MENTAL HEALTH OF CHILDREN: A TWIN STUDY.

#### Yin P. Hou X. Qin Q. et al.

The current study explored the influences of genetic and environmental factors on the mental health of twins between ages 6 and 16. A total of 41 monozygotic (MZ) twins and 35 dizygotic twins were recruited. The psychological attributes and environmental information of children were evaluated. A significant correlation was found between twins in the diagnostic categories of any psychiatric disorder and attention deficit/hyperactivity disorder (ADHD)/hyperkinesis based on the Strengths and Difficulties Questionnaire scale in MZ twins. Furthermore, fathers' authoritarian parenting style was positively correlated with the probability of any psychiatric disorders and oppositional/conduct disorders, whereas mothers' authoritative parenting style was negatively correlated with the probability of any psychiatric disorders and ADHD/hyperkinesis. The probability of emotional disorders was negatively correlated with scores on the

Stressful Life Events Scale. These results collectively suggest that genetic and environmental elements, such as parental rearing style and stressful life events, may influence children's mental health

.....

J Youth Adolesc. 2017 Jul;46:1424-51.

RACIAL/ETHNIC DISPROPORTIONALITY IN PSYCHIATRIC DIAGNOSES AND TREATMENT IN A SAMPLE OF SERIOUS JUVENILE OFFENDERS.

Baglivio MT, Wolff KT, Piquero AR, et al.

Psychiatric disorder prevalence has been shown demonstrably higher among justice-involved adolescents than youth in the general population. Yet, among arrested juveniles, little is known regarding racial/ethnic differences in disorder prevalence, the role of trauma exposure in the diagnosis of behavioral disorders, or subsequent psychiatric treatment provided to adolescents with such diagnoses. The current study examines racial/ethnic disparity in psychiatric diagnoses and treatment of behavioral disorders associated with delinquency, controlling for traumatic experiences, behavioral indicators, and prior offending among serious juvenile offenders. Logistic regression is employed to explore the racial/ethnic disproportionality in behavioral disorder diagnoses and psychiatric treatment provision among 8763 males (57.7 % Black, 11.8 % Hispanic) and 1,347 females (53.7 % Black, 7.6 % Hispanic) admitted to long-term juvenile justice residential placements in Florida. The results indicate Black males are 40 % more likely, and Black females 54 % more likely to be diagnosed with conduct disorder than Whites, even upon considerations of trauma, behavioral indicators, and criminal offending. Black and Hispanic males are approximately 40 % less likely to be diagnosed with ADHD than White males, with no racial/ethnic differences for females. Importantly, Black males are 32 % less likely to receive psychiatric treatment than White males, with no differences between White and Hispanic males, or any female subgroups. Traumatic exposures increased the odds of oppositional defiant disorder and ADHD, but not conduct disorder for males, though adverse childhood experiences were unrelated to behavioral disorder diagnoses among females

.....

JAMA. 2018 Mar:319:1113-24.

QUALITY OF HEALTH CARE FOR CHILDREN IN AUSTRALIA, 2012-2013.

Braithwaite J, Hibbert PD, Jaffe A, et al.

**Importance**: The quality of routine care for children is rarely assessed, and then usually in single settings or for single clinical conditions. Objective: To estimate the quality of health care for children in Australia in inpatient and ambulatory health care settings.

**Design, Setting, and Participants**: Multistage stratified sample with medical record review to assess adherence with quality indicators extracted from clinical practice guidelines for 17 common, high-burden clinical conditions (noncommunicable [n = 5], mental health [n = 4], acute infection [n = 7], and injury [n = 1]), such as asthma, attention-deficit/hyperactivity disorder, tonsillitis, and head injury. For these 17 conditions, 479 quality indicators were identified, with the number varying by condition, ranging from 9 for eczema to 54 for head injury. Four hundred medical records were targeted for sampling for each of 15 conditions while 267 records were targeted for anxiety and 133 for depression. Within each selected medical record, all visits for the 17 targeted conditions were identified, and separate quality assessments made for each. Care was evaluated for 6689 children 15 years of age and younger who had 15240 visits to emergency departments, for inpatient admissions, or to pediatricians and general practitioners in selected urban and rural locations in 3 Australian states. These visits generated 160202 quality indicator assessments.

**Exposures**: Quality indicators were identified through a systematic search of local and international guidelines. Individual indicators were extracted from guidelines and assessed using a 2-stage Delphi process.

Main Outcomes and Measures: Quality of care for each clinical condition and overall.

**Results**: Of 6689 children with surveyed medical records, 53.6% were aged 0 to 4 years and 55.5% were male. Adherence to quality of care indicators was estimated at 59.8% (95% CI, 57.5%-62.0%; n = 160202) across the 17 conditions, ranging from a high of 88.8% (95% CI, 83.0%-93.1%; n = 2638) for autism to a low

of 43.5% (95% CI, 36.8%-50.4%; n=2354) for tonsillitis. The mean adherence by condition category was estimated as 60.5% (95% CI, 57.2%-63.8%; n=41265) for noncommunicable conditions (range, 52.8%-75.8%); 82.4% (95% CI, 79.0%-85.5%; n=14622) for mental health conditions (range, 71.5%-88.8%); 56.3% (95% CI, 53.2%-59.4%; n=94037) for acute infections (range, 43.5%-69.8%); and 78.3% (95% CI, 75.1%-81.2%; n=10278) for injury.

**Conclusions and Relevance**: Among a sample of children receiving care in Australia in 2012-2013, the overall prevalence of adherence to quality of care indicators for important conditions was not high. For many of these conditions, the quality of care may be inadequate

.....

J Abnorm Child Psychol. 2018 Feb;46:265-76.

#### PREDICTING ADHD SYMPTOMS IN ADOLESCENCE FROM EARLY CHILDHOOD TEMPERAMENT TRAITS.

## Einziger T, Levi L, Zilberman-Hayun Y, et al.

Extreme levels of certain temperament traits can be early markers of different developmental pathways of attention-deficit/hyperactivity disorder (ADHD). However, the long-term utility of using these traits as predictors of ADHD is not fully known. This study includes 64 male adolescents (M age = 13.5), who have been followed since birth as part of a longitudinal study. The primary aim was to test effortful control (EC), activity level, and anger, measured in early childhood – both with mother's reports and laboratory assessments –as predictors of ADHD symptoms in adolescence. Further, we investigated the specificity of this prediction to the different ADHD symptom domains. The results demonstrated that early temperament dimensions of EC and activity level were predictive of ADHD symptoms about 10 years later, when the participants reached adolescence. Moreover, activity level showed specificity only to hyperactivity-impulsivity symptoms whereas EC was a predictor of the two symptom domains. Anger had a predictive correlation with ADHD symptoms; however, it did not have a unique predictive contribution. These results emphasize the relevance of EC and activity level in the developmental course of ADHD. Identification of early risk factors can lead to more efficient design and implementation of intervention programs

.....

J Abnorm Child Psychol. 2018 Feb;46:277-90.

LOW WORKING MEMORY RATHER THAN ADHD SYMPTOMS PREDICTS POOR ACADEMIC ACHIEVEMENT IN SCHOOL-AGED CHILDREN.

#### Simone AN, Marks DJ, Bédard AC, et al.

This study examined whether working memory (WM), inattentive symptoms, and/or hyperactive/impulsive symptoms significantly contributed to academic, behavioral, and global functioning in 8-year-old children. One-hundred-sixty 8-year-old children (75.6% male), who were originally recruited as preschoolers, completed subtests from the Wechsler Intelligence Scale for Children-Fourth Edition, Integrated and Wechsler Individual Achievement Test-Second Edition to assess WM and academic achievement, respectively. Teachers rated children's academic and behavioral functioning using the Vanderbilt Rating Scale. Global functioning, as rated by clinicians, was assessed by the Children's Global Assessment Scale. Multiple linear regressions were completed to determine the extent to which WM (auditory-verbal and visualspatial) and/or inattentive and hyperactive/impulsive symptom severity significantly contributed to academic, behavioral, and/or global functioning. Both auditory-verbal and visual-spatial WM but not ADHD symptom severity, significantly and independently contributed to measures of academic achievement (all p < 0.01). In contrast, both WM and inattention symptoms (p < 0.01), but not hyperactivity-impulsivity (p > 0.05) significantly contributed to teacher-ratings of academic functioning. Further, inattention and hyperactivity/impulsivity (p < 0.04), but not WM (p > 0.10) were significantly associated with teacher-ratings of behavioral functioning and clinician-ratings of global functioning. Taken together, it appears that WM in children may be uniquely related to academic skills, but not necessarily to overall behavioral functioning

J Abnorm Child Psychol. 2018 Feb;46:251-63.

GENE-ENVIRONMENT INTERACTIONS IN ADHD: THE ROLES OF SES AND CHAOS.

# Gould KL, Coventry WL, Olson RK, et al.

Although attention-deficit/hyperactivity disorder (ADHD) is highly heritable, emerging evidence suggests symptoms are associated with interactions between genes and the environment (GxE) during development. This study tested whether heritability of ADHD symptoms is moderated by two environmental factors: socioeconomic status (SES) and chaos (household disorganisation). A population sample of 520 twin pairs (N = 1040, 52.3% female) from 6 to 15 years completed measures of behavior and home environment. Structural equation modelling was then used to test whether environmental factors were associated with a change in the extent to which genes explain variability in ADHD symptoms. Neither chaos nor SES moderated heritability, with consistent contributions from both genes and environment indicated across socioeconomic strata and levels of chaos. This finding contrasts with those of previous research, underlining the need to replicate results in the emerging field of GxE research across different populations and statistical methods. Robust findings may assist in developing targeted interventions for genetically vulnerable individuals

.....

J Child Neurol. 2018.

THE SHORT-TERM PLACEBO RESPONSE IN CHILDREN WITH ATTENTION-DEFICIT HYPERACTIVITY DISORDER (ADHD).

#### Cohen A, Plonsky-Toder M, Tirosh E.

To assess short-term placebo response in 6- to 13-year-old children with ADHD, children who were administered a double-blind placebo-methylphenidate trial, 1 week each, were included in the analysis. Conners ΓÇÖ parents and Teacher Rating scales, the Aggregate Neurobehavioral Student Health and Educational Review inventory, and the Matching Familiar Figure Test were employed. A reduction of 30% or more in one or more of the teachers report subscales was observed in 18.8% of the participants. Attention test performance resulted in 58% of children exhibiting reduction in error rates and 36.2% exhibited longer latency period. Significant correlations between placebo response and methylphenidate response in all of the teachers report subscales were found. Base line severity, learning problem and emotional status were found associated with placebo response. Short-term placebo response should be accounted for in children with ADHD

.....

J Child Psychol Psychiatry. 2018 Mar;59:203-12.

FROM POSITIVE PSYCHOLOGY TO PSYCHOPATHOLOGY: THE CONTINUUM OF ATTENTION-DEFICIT HYPERACTIVITY DISORDER.

## Greven CU, Buitelaar JK, Salum GA.

**Background**: Integration of positive psychology into clinical research and treatment has been slow. This integration can be facilitated by the conceptualisation of mental disorders as the high, symptomatic extreme of continuous normal variation. This assumes that there is also a low, positive extreme, which is, however, unchartered territory. This study aims to examine how well current measures capture the low extreme of mental disorder continua, using attention-deficit hyperactivity disorder (ADHD) as an example.

**Methods**: The ability of three validated scales to capture ADHD as a continuous trait was examined using Item Response Theory in a sample of 9,882 adolescents from the UK population-representative Twins Early Development Study. These scales were: the Strengths and Weakness of ADHD Symptoms and Normal behaviour scale (SWAN), Strength and Difficulties Questionnaire (SDQ—hyperactivity subscale), and Conners' Parent Rating Scale (Conners).

**Results**: Only the SWAN reliably differentiated interindividual differences between participants lying at any level of the continuous ADHD latent trait, including the extreme low, positive end (z-scores from - 3 to + 3). The SDQ showed low reliability across the ADHD latent trait. In contrast, the Conners performed best at differentiating individuals scoring at or above the mean to the high symptomatic range (z-scores from 0 to +

3). The SWAN was the only measure to provide indicators of 'positive mental health', endorsed in the presence of particularly good attentive abilities.

**Conclusions**: Scales such as the SWAN that reliably capture ADHD as a continuous trait, including the positive end, are important for not missing meaningful variation in population-based studies. Indicators of positive mental health may be helpful in clinical practice, as positive attributes have been shown to directly influence as well as buffer negative effects of psychiatric symptoms

.....

J Child Psychol Psychiatry. 2018 Mar; 59:285-95.

EXPLAINING THE RELATIONSHIP BETWEEN TEMPERAMENT AND SYMPTOMS OF PSYCHIATRIC DISORDERS FROM PRESCHOOL TO MIDDLE CHILDHOOD: HYBRID FIXED AND RANDOM EFFECTS MODELS OF NORWEGIAN AND SPANISH CHILDREN.

## Wichstrøm L, Penelo E, Rensvik Viddal K, et al.

**Background**: Four explanations for the concurrent and prospective associations between temperament and psychopathology in children have been suggested: predisposition, complication/scar, common cause/continuity, and pathoplasty/exacerbation. Because the confounding effects of common causes have not been ruled out in prior work, the support for the various explanations is uncertain.

**Methods**: Screen-stratified community samples of 4-year olds in Trondheim, Norway (n = 1,042), and 3-year olds in Barcelona, Spain (n = 622), were assessed biennially for symptoms of attention-deficit/hyperactivity (ADHD), oppositional defiant (ODD), conduct (CD), anxiety, and depressive disorders through interviewer-based psychiatric interviews across four waves of data collection. The parents completed child temperament ratings. The data were analyzed with random and fixed effects regression adjusted for all time-invariant unmeasured confounders (e.g., genetics, common methods bias, item overlap).

**Results**: In both Norway and Spain and across ages, negative affect predisposed children to symptoms of all disorders except CD, low effortful control predisposed children to ADHD and ODD-symptoms, and surgency predisposed children to increased ADHD-symptoms. Complication effects were observed in the Spanish children for ADHD-symptoms, which increased surgency and diminished effortful control, and for ODD-symptoms, which decreased surgency. The common cause and pathoplasty/exacerbation explanations were not supported.

**Conclusions**: The present results are consistent with the view that temperament plays a causal role in the development of symptoms of psychiatric disorders in children. Because temperament is malleable, interventions targeting the affective, attentional, and behavioral regulatory components of temperament may reduce psychopathology in children

.....

J Clin Child Adolesc Psychol. 2018 Mar;47:248-65.

HIGH VERSUS LOW INTENSITY SUMMER TREATMENT FOR ADHD DELIVERED AT SECONDARY SCHOOL TRANSITIONS. Siblev MH. Coxe SJ. Campez M. et al.

Spikes in symptom severity are noted for adolescents with attention deficit/hyperactivity disorder (ADHD) at the transitions to middle and high school that are attributed to developmental maladjustment. This study evaluated the effectiveness of high-intensity (HI; 412 hr, \$4,373 per participant) versus low-intensity (LI; 24 hr, \$97 per participant) skills-based summer intervention delivered to adolescents with ADHD by local school district staff. Participants were 325 ethnically diverse rising sixth and ninth graders with ADHD randomized to HI versus LI (n = 218) or recruited into an untreated comparison group (n = 107). Group × Time 1-year outcome trajectories were compared using linear mixed models. Both interventions possessed high fidelity and were viewed by families as enjoyable and beneficial. Youth attendance was higher for HI (~80%) versus LI (~45%). Parent training attendance was uniform across groups (~50%). Parent and student attendance did not impact trajectories. Primary benefits of HI over LI were to note taking (d = .50), parent contingency management (d = .43), and parent-rated ADHD symptoms (d = .40–.46; ninth grade only). Secondary analyses suggested that HI may produce additional benefits compared to no treatment for home organization skills (HI vs. untreated d = .54), parent–teen conflict (HI vs. untreated d = .39), and grade point average (HI

vs. untreated d = .47, ninth grade only). Summer HI treatment was superior to LI in engagement and uptake of certain skills. However, the extent to which these medium benefits on a limited number of outcomes justify high costs compared to LI remains an open question. Delivering treatment during the summer instead of school year may limit generalizability. (PsycINFO Database Record (c) 2018 APA, all rights reserved)

.....

J Clin Child Adolesc Psychol. 2018 Mar;47:213-35.

SOCIAL FUNCTIONING IN CHILDREN WITH OR AT RISK FOR ATTENTION DEFICIT/HYPERACTIVITY DISORDER: A META-ANALYTIC REVIEW.

#### Ros R, Graziano PA.

Considerable work has demonstrated significant impairment in social functioning for children with attention deficit/hyperactivity disorder (ADHD). The social functioning profiles of children with ADHD are marked by impairments across diverse domains as they tend to experience greater rates of peer rejection, have lower levels of social skills, and have impaired social cognitions. The purpose of this study was to (a) quantitatively examine the association between ADHD and deficits across several domains of social functioning (peer functioning, social skills, social information processing), (b) examine differences in the magnitude of such associations, and (c) examine the effect of potential moderators. A meta-analysis of 109 studies (n = 104,813) revealed that children with ADHD have the most impairment within the peer functioning domain (weighted effect size [ES] r = .33) followed by significantly smaller effects within the social skills (weighted ES r = .27) and social information-processing domains (weighted ES r = .27). When examining potential moderators, results revealed that the association between ADHD and deficits within the social skills domain was weaker among studies that controlled for co-occurring conduct problems (CP). Studies that utilized sociometric and teacher reports of peer status reported the largest effects within the peer functioning domain. In addition, studies that utilized the 'gold standard' approach to diagnosing ADHD documented the largest effects within both the social skills and peer functioning domains. Last, studies utilizing younger samples revealed the largest effects for deficits within the peer functioning domain. Theoretical and clinical implications are discussed

.....

J Clin Child Adolesc Psychol. 2018 Mar;47:199-212.

PREVALENCE OF PARENT-REPORTED ADHD DIAGNOSIS AND ASSOCIATED TREATMENT AMONG U.S. CHILDREN AND ADOLESCENTS, 2016.

# Danielson ML, Bitsko RH, Ghandour RM, et al.

The purpose of this study is to estimate the national prevalence of parent-reported attention deficit/hyperactivity disorder (ADHD) diagnosis and treatment among U.S. children 2–17 years of age using the 2016 National Survey of Children's Health (NSCH). The NSCH is a nationally representative, cross-sectional survey of parents regarding their children's health that underwent a redesign before the 2016 data collection. It included indicators of lifetime receipt of an ADHD diagnosis by a health care provider, whether the child currently had ADHD, and receipt of medication and behavioral treatment for ADHD. Weighted prevalence estimates were calculated overall and by demographic and clinical subgroups (n = 45,736). In 2016, an estimated 6.1 million U.S. children 2–17 years of age (9.4%) had ever received an ADHD diagnosis. Of these, 5.4 million currently had ADHD, which was 89.4% of children ever diagnosed with ADHD and 8.4% of all U.S. children 2–17 years of age. Of children with current ADHD, almost two thirds (62.0%) were taking medication and slightly less than half (46.7%) had received behavioral treatment for ADHD in the past year; nearly one fourth (23.0%) had received neither treatment. Similar to estimates from previous surveys, there is a large population of U.S. children and adolescents who have been diagnosed with ADHD by a health care provider. Many, but not all, of these children received treatment that appears to be consistent with professional guidelines, though the survey questions are limited in detail about specific treatment types

Newsletter – ADHD marzo 2018

received. The redesigned NSCH can be used to annually monitor diagnosis and treatment patterns for this highly prevalent and high-impact neurodevelopmental disorder

.....

J Clin Child Adolesc Psychol. 2018 Mar;47:336-44.

NEURAL PROCESSING OF THREAT CUES IN YOUNG CHILDREN WITH ATTENTION-DEFICIT/HYPERACTIVITY SYMPTOMS. Flegenheimer C, Lugo-Candelas C, Harvey E, et al.

A growing literature indicates that attention deficit/hyperactivity disorder (ADHD) involves difficulty processing threat-related emotion faces. This deficit is especially important to understand in young children, as threat emotion processing is related to the development of social skills and related behavioral regulation. Therefore, the current study aimed to better understand the neural basis of this processing in young children with ADHD symptoms. Forty-seven children between 4 and 7 years of age were included in the analysis, 28 typical developing and 19 with clinically significant levels of ADHD hyperactive/impulsive symptoms. Participants completed a passive affective face-viewing task. Event-related potentials were assessed for each emotion, and parental report of child behavior and emotion regulation abilities was assessed. Children with ADHD symptoms showed altered N170 modulation in response to specific emotion faces, such that the N170 was less negative in response to fearful compared to neutral faces, whereas typically developing children showed the opposite pattern. Groups did not differ in reactivity to anger or non-threat-related emotion faces. The N170 difference in fearful compared to neutral faces correlated with reported behavior, such that less fear reactivity predicted fewer prosocial behaviors. Abnormalities in the underlying neural systems for fear processing in young children with ADHD symptoms may play an important role in social and behavioral deficits within this population

.....

J Clin Psychopharmacol. 2018;38:159-61.

ARIPIPRAZOLE TREATMENT OF COMPULSIVE BEHAVIORS ASSOCIATED WITH METHYLPHENIDATE IN A CHILD WITH DOWN SYNDROME.

Sertdemir M, Akça ÖF.

.....

J Med Biol Eng. 2018;38:138-49.

CAN FUNCTIONAL CONNECTIVITY AT RESTING BRAIN IN ADHD INDICATE THE IMPAIRMENTS IN SENSORY-MOTOR FUNCTIONS AND FACE/EMOTION RECOGNITION?

Icer S, Benli SG, Gumus K, et al.

Attention deficit hyperactivity disorder (ADHD) is a neurodevelopmental disease known to cause impairments in cognitive, sensory-motor functions and face/emotion recognition. This study aimed to examine the restingstate brain networks in children with ADHD using functional magnetic resonance imaging. We performed seed-to-voxel and region of interest (ROI) analyses including all Broadmann areas (BAs) comprehensively. Thirty right-handed children aged between 9 and 16-áyears (15 with ADHD and 15 typically developing control subjects closely matched for age and gender) were included. Ninety five brain regions including 84 BAs and 11 Default Mode network (DMN)-related regions (rsREL) were studied using seed-based and ROIto-ROI analysis and connectivity measures were calculated (p-áOpenSPiltSPi-á0.001). Between-group differences were assessed by using t-statistics (p-áOpenSPiltSPi-á0.05). Seed-based analysis showed connectivity differences in the sensory-motor and face/emotion recognition regions in both groups. The between-group whole-brain comparison showed greater magnitude of activation in children with ADHD than in control subjects in brain regions that included the face/emotion recognition system and prefrontal cortex based on ROI-to-ROI analysis. This work revealed that the sensory-motor regions and regions related to face/emotion recognition showed atypical functional connectivities in ADHD patients compared to the controls. Observation of the differences in these regions supports previous findings in the literature based on task-based functional magnetic resonance imaging (fMRI) studies. Our study exhibited that these atypical differences can also occur in the resting brain. These results suggest that further investigations of regions related to motor-sensory and face/emotion recognition are required to better understand ADHD

.....

Journal of Medicinal Plants. 2018;17:1-6.

ATTENTION-DEFICIT/HYPERACTIVITY DISORDER AND HERBAL MEDICINE: AN EVIDENCED BASED APPROACH. Akhondzadeh S.

Attention-Deficit/Hyperactivity Disorder (ADHD) is one of the most common psychiatric disorders in children and adolescents with a worldwide prevalence of 5%. It is characterized by symptoms of attention deficit and/or hyperactivity/impulsiveness that is maintained for at least six months. ADHD is a neural disorder with structural and functional abnormalities in some areas of the brain. Pharmacotherapy is the most prevalent treatment for all age groups of ADHD patients. ADHD is amenable to drugs that affect the catecholaminergic neurotransmitter pathways among which stimulants stand out. In spite of the fact that stimulants are the most used drugs among current standard treatments and are generally safe and highly effective, they could be associated with unresponsiveness and significant side effects such as sleep disturbances, decreased appetite and mood lability in some children. Sleep problems are suggested to be not only a side effect for current standard treatments but also a common finding in patients with ADHD. Moreover, there is growing interest regarding herbal medicine in the treatment of ADHD. This review focuses on some herbal medicines in ADHD

.....

J Neuropsychiatry Clin Neurosci. 2017;29:e19-e20.

A CASE OF ATTENTION DEFICIT HYPERACTIVE DISORDER COMPLICATED WITH THREE OTHER CO-MORBIDITIES THAT RISPERIDONE-LAI WAS EFFECTIVE IN CONTROLLING IMPULSIVITY.

## Oishi K, Tamura M, Okato A, et al.

**Background**: Attention deficit hyperactivity disorder (ADHD) is a common psychiatric disorder frequently characterized by inattention, impulsivity and hyperactivity. In an absence of adequate treatments, ADHD could severely impede both academic and social performance. Although ADHD is generally well responsive to medications, its potent comorbidities such as oppositional or conduct, mood and developmental disorders often impair patients' adherences. We here describe the case of ADHD that risperidone long-acting injection (RLAI) was effective to control impulsivity.

Case History: The patient was a Japanese 12 years old girl, whose chief compliant were inattentiveness and impulsivity. She had a history of repeated exposure to alcohol during prenatal period and domestic violence since early childhood. Both parents were diagnosed to bipolar disorder and alcoholism while her only sister had depression. Through clinical assessments, we found that she met the diagnostic criterion, according to the 5th American Psychiatric Association's Diagnostic and Statistical Manual of Mental Disorders (DSM-5), of ADHD and comorbid disorders including oppositional defiant disorder, reactive attachment disorder and Tourette syndrome. Atomoxetine showed insufficient effectiveness to control impulsivity, although we observed the clear improvement when risperidone was medicated. However, her inattentiveness and behavioral difficulties were the major limitation for the continuation of oral medications. Conclusion: We observed that the use of RLAI for 12-year-old ADHD patient with complex comorbidities

overcame the limitation in adherence and resulted in the improvement of hardly controlled impulsivity. This case shows that LAI would make an alternative candidate for medications especially when patients have difficulties in maintaining reliable adherence

J Pediatr. 2018.

ATTENTION DEFICIT HYPERACTIVITY DISORDER IN CHILDHOOD: HEALTHCARE USE IN A DANISH BIRTH COHORT DURING THE FIRST 12 YEARS OF LIFE.

Laugesen B, Mohr-Jensen C, Boldsen SK, et al.

**Objectives**: To compare the mean number of medical and psychiatric hospital-based services in children with and without attention deficit hyperactivity disorder (ADHD) and to assess the effect of ADHD on hospital-based service use, including child-, parental-, and socioeconomic-related risk factors.

**Study design**: A Danish birth cohort was followed through 12 years, and children with ADHD were identified using Danish nationwide registries. Poisson regression analyses were used to assess the association of ADHD with service use and to adjust for a comprehensive set of explanatory variables.

**Results**: Children diagnosed with ADHD used more medical and psychiatric hospital-based healthcare than those without ADHD. In children with ADHD, intellectual disability and parental psychiatric disorder were associated with increased medical and psychiatric service use. Low birth weight and low gestational age were associated with increased medical service use. Psychiatric comorbidity and having a divorced or single parent were associated with increased psychiatric service use.

**Conclusions**: ADHD independently affected medical and psychiatric hospital-based service use even when adjusting for a comprehensive set of explanatory variables. However, the pattern of medical and psychiatric hospital-based service use is complex and cannot exclusively be explained by the child-, parental-, and socioeconomic-related variables examined in this study

.....

J Psychiatr Res. 2018;101:42-49.

ADHD, DEPRESSION, AND MOTOR VEHICLE CRASHES: A PROSPECTIVE COHORT STUDY OF CONTINUOUSLY-MONITORED, REAL-WORLD DRIVING.

Aduen PA, Kofler MJ, Sarver DE, et al.

ADHD is associated with automobile crashes, traffic fatalities, and serious road trauma, but it is unclear whether this risk is (a) driven by ADHD symptoms specifically, and (b) unique to ADHD or transdiagnostic across psychiatric disabilities, such as depression, that also have concentration problems as core symptoms. The current study provides the first prospective, continuously-monitored evaluation of crash risk related to ADHD symptoms, including the first on-road comparison of ADHD with another high-prevalence psychiatric disability (depression). A probability-based sample of 3226 drivers from six U.S. sites, including subsamples with self-reported ADHD (n = 274) and depression (n = 251), consented to have their vehicles outfitted with sophisticated data acquisition technologies to continuously monitor real-world, day-to-day driving from ΓÇÿengine-on to engine-offΓÇÖ for 1ΓÇô2 years (Mean = 440 consecutive days/driver, Mean = 9528 miles/driver). Crashes and near-crashes were objectively identified via software-based algorithms and double-coded manual validation (blinded to clinical status). Miles driven, days monitored, age, gender, education, and marital status were controlled. ADHD symptoms portended 5% increased crash risk per increase in symptom severity score (IRR = 1.05). This risk corresponded to approximately 1 biennial crash and 1 annual near-crash per driver with ADHD; crash risk doubled for drivers reporting ADHD symptom severity near the sample's maximum. Analyses based on self-reported clinical status indicated similarly elevated rates for ADHD (IRR = 1.46) and depression (IRR = 1.34) that may be related, in part, to both groups' inattention/concentration symptoms. Risk was not attenuated by ADHD usual treatment, but varied according to antidepressant medication status. Previous studies have significantly underestimated the risk for traffic crashes conveyed by ADHD and depression

.....

J Psychoeduc Assess. 2018 Mar;36:136-47.

INFORMANT DISCREPANCIES IN THE ASSESSMENT OF ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.

Kennerley S. Jaquiery B. Hatch B. et al .

An attention-deficit/hyperactivity disorder (ADHD) diagnosis requires symptoms to be present across two or more settings, thus requiring information from multiple informants. Research consistently shows low to

moderate agreement between parents and teachers; however, the mechanisms underlying these discrepancies remain unclear. This study examined (a) agreement between parents and teachers, (b) effects of using different combination rules in assigning diagnoses, and (c) the role of contextual influences and/or personal biases in informants' reports. Fifty-five children, their parents, and teachers participated. Parent and teacher ratings on the Attention-Deficit/Hyperactivity Disorder Rating Scale—Fourth edition (ADHD-RS-IV) and clinician ratings on the Behavioral Observation of Students in Schools (BOSS) were obtained. Results indicated moderate agreement among parent and teacher ratings on the ADHD-RS. Diagnostically, the rule for combining information from multiple informants dramatically altered the ADHD classification assigned to the child. With regard to rater differences, the clinician-rated school observation gave some support for the notion that ratings are person rather than context specific

.....

J Psychopathol Behav Assess. 2018;40:26-39.

PSYCHOPATHIC PERSONALITY WORKS BETTER THAN CU TRAITS FOR PREDICTING FEARLESSNESS AND ADHD SYMPTOMS AMONG CHILDREN WITH CONDUCT PROBLEMS.

# Frogner L, Andershed A-K, Andershed H.

Children with early-onset conduct problems (CP) are at great risk for future behavior problems, and this risk seems to increase when CP co-occur with psychopathic traits. Even though studies are indicating that the entire psychopathic personality construct may be more useful in designating a meaningful subgroup of children with CP, research on psychopathic traits and CP in childhood have mainly focused on the role of callous unemotional (CU) traits. Prospective longitudinal data of 1867 3- to 5-year-olds (47% girls) followed annually for two years was used to compare groups of children with different combinations of CP and psychopathic traits on fearlessness and Attention-Deficit Hyperactivity Disorder (ADHD) symptoms. Children with CP and psychopathic personality had higher baseline and stable levels of ADHD symptoms than children with CP only or children with CP and concurrent CU traits, while baseline levels of fearlessness did not differ. They were also more likely to display stable levels of the risky combination of CP and ADHD symptoms. Results were similar for boys and girls. Findings indicate that there are reasons to consider other traits and behaviors as specifiers for subgroups of children with CP over and above CU traits, in order to optimize both diagnostic practice and treatment outcomes

J SLEEP RES. 2018.

DISTURBED SLEEP AND ACTIVITY IN TODDLERS WITH EARLY SIGNS OF ATTENTION DEFICIT HYPERACTIVITY DISORDER (ADHD).

.....

#### Bundgaard A-K, Asmussen J, Pedersen NS, et al.

This study investigated whether early signs of attention deficit hyperactivity disorder (ADHD) in toddlers aged 2-3 years are associated with disturbed sleep and activity levels. Participants were recruited from the Odense Child Cohort, and children scoring above the 93rd percentile on the ADHD scale of the Child Behaviour Checklist 11/2-5 were categorised as cases and compared with age- and gender-matched normal-scoring controls. Daytime and nocturnal activity for 24 children with ADHD traits (cases) and 25 healthy controls was assessed through 7 days of actigraphy, and parents completed the Children's Sleep Habits Questionnaire (CSHQ) and the ADHD Rating Scale IV Preschool Version (ADHD-RS). Cases differed significantly on actigraphic parameters by having fewer minutes of moderate-to-vigorous physical activity (MVPA), prolonged total sleep time, fewer sleep interruptions, and increased night-to-night variability. A significant association was found between fewer minutes of MVPA and higher parent-reported motor activity on the ADHD-RS. Furthermore, increased night-to-night variability was significantly associated with higher total scores on both CSHQ and ADHD-RS. The findings show that early signs of ADHD are associated with an irregular sleep pattern and lower daytime activity, as illustrated by actigraphy. Studies investigating early ADHD risk factors could lead to a preschool ADHD risk index to help guide future early intervention

J Am Acad Child Adolesc Psychiatry. 2018 Mar;57:175-82.

WORKING MEMORY AND VIGILANCE AS MULTIVARIATE ENDOPHENOTYPES RELATED TO COMMON GENETIC RISK FOR ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.

# Nigg JT, Gustafsson HC, Karalunas SL, et al.

**Objective**: Understanding the role of endophenotypes is essential for process models of psychopathology. This study examined which candidate cognitive endophenotypes statistically mediate common variant genetic risk for attention-deficit/hyperactivity disorder (ADHD).

**Method**: A case-control design using community-recruited volunteer children 7 to 11 years of age (n = 656, n = 435 ADHD), of whom 514 were of homogenous European ancestry for the primary models (n = 337 ADHD, 177 non-ADHD). Children were assessed with a multi-informant, best-estimate diagnostic procedure and laboratory measures of working memory, response inhibition, executive functioning, arousal/attention, temporal information processing, and processing speed. Latent variables were created for the candidate cognitive measures and for parent- and teacher-rated ADHD dimensions. Polygenic risk scores (PGS) were computed using a discovery sample of 20,183 individuals with ADHD and 35,191 controls from the Psychiatric Genetics Consortium. Cognitive measures that survived multiple testing correction for association with the PGS were evaluated for mediation with ADHD using structural equation models.

**Results**: Results were essentially identical in the homogeneous European ancestry subgroup (n = 514) and in the full sample (N = 656). For the European population, the PGS was associated with ADHD diagnosis (Nagelkerke R² = 0.045;  $\beta$  = 0.233, SE = 0.053, p = .000011) and multi-indicator dimensional ADHD latent variables by parent report ( $\beta$  = 0.185, SE = 0.043) and teacher report ( $\beta$  = 0.165, SE = 0.042). The PGS effect was statistically mediated by working memory (indirect effect,  $\beta$  = 0.101, SE = 0.029, 95% CI = 0.05, 0.16, p = .00049, 43% of genetic effect accounted for) and arousal/alertness (indirect effect  $\beta$  = 0.115, 95% CI = 0.04, 0.20, SE = 0.041, p = .005, 49% of genetic effect accounted for).

**Conclusion**: This is the first clear demonstration from molecular genetic data that working memory and arousal regulation are promising cognitive endophenotypes for ADHD with regard to mediating genetic risk from common genetic variants

.....

Journal of the Chinese Medical Association. 2018;81:277-83.

ASSOCIATION BETWEEN ALLERGIC DISEASES, ALLERGIC SENSITIZATION AND ATTENTION-DEFICIT/HYPERACTIVITY DISORDER IN CHILDREN: A LARGE-SCALE, POPULATION-BASED STUDY.

# Yang C-F, Yang C-C, Wang I-J.

**Background**: Increasing prevalence of allergic diseases has been matched by parallel trends in attention-deficit/hyperactivity disorder (ADHD). However, previous studies concerning the association between ADHD and allergic diseases have been inconsistent. Moreover, it is not clear whether this association is modified by allergic sensitization status. Therefore, we evaluated the association between allergic diseases, allergic sensitization, and ADHD in children.

**Methods**: We conducted a large-scale cross-sectional, population-based survey to investigate the relationship between allergic diseases, allergic sensitization, and ADHD. Children aged between 3 and 6 years were selected from kindergartens, and received skin prick tests (SPTs) for mite, cockroach, dog, milk, egg, and crab allergens. Information about allergic diseases, environmental exposures, and physician-diagnosed ADHD were collected. Multiple logistic regressions were performed to estimate the association between allergic diseases and ADHD, with adjustments made for potential confounders.

**Result**: A total of 2772 children were found to be eligible for analysis; of these 411 (14.8%) had atopic dermatitis (AD), 954 (34.4%) had allergic rhinitis (AR), 451 (16.3%) had asthma, and 28 (1.01%) had ADHD. Children who had AD and asthma with allergic sensitization were found to be at increased risk for ADHD, with adjusted ORs (95% CI) of 4.50 (1.28ΓÇô15.86) and 3.65 (1.07ΓÇô12.49). Children who had AR, allergic conjunctivitis, or food allergies were also related to ADHD, though failed to reach statistical significance.

**Conclusion**: Our results suggest that AD and asthma with allergic sensitization are associated with ADHD in children. As allergic sensitization is an increased factor of developing allergic diseases, early control of environmental and allergens exposure could help to modify the burden of ADHD

Minerva Psichiatrica. 2018;59:29-38.

COMPARISON OF THREE METHODS OF INTERVENTION PHARMACOTHERAPY, COGNITIVE-MOTION REHABILITATION AND THE COMBINATION ON COMPONENTS OF ATTENTION OF DD CHILDREN.

Shamshiri S, Sheikh M, Hemayat TR, et al.

**BACKGROUND**: Attention-deficit/hyperactivity disorder (ADHD) is one of the most common disorders in childhood and adolescence and it is of particular importance to find eff ff ective treatment which can diminish the intensity and depth as symptoms. This study is aimed to compare three methods of intervention cognitive-motion rehabilitation, pharmacotherapy and the combination of two paths to alleviate the components of attention of children with attention deficit / hyperactivity disorder (combined type).

**METHODS**: This study is a kind of Quasi-experimental and prospective study including three groups: pretest - post-Test - follow-up tests. Using stratified cluster random method 35 schools were selected from schoolboys in Dezful city and then using Conners Scale (Parent and teacher form) and diagnosis of Child and Adolescent Psychiatrist, 45 children 7 to 11 years old with ADHD were identified in Prototype and after synchronization of intelligence, randomly divided into three experimental groups (cognitive-motion group, drug therapy group and combined group). IVA + PLUS Test and Scale Wechsler Digit Span Test were used in three phases. Data collected using tests covariance univariate and Bonferroni post-hoc test were processed.

**RESULTS**: The combination group in selective attention, focused attention and divided attention did better than the other two groups at post-Test. Also were not much different in sustained attention and alternative attention between three groups. Study of changes during follow-up revealed that both combined and cognitive-motion rehabilitation groups had a significant improvement in attention variables than pharmacotherapy group. In fact, the medication group, unlike the other two groups had roughly the same decline in performance as the pretest.

**CONCLUSIONS**: The results suggest that combination of treatment protocol cognitive-motion rehabilitation with low dose of medicine has more and more lasting effects than pharmacotherapy

.....

Mol Psychiatry. 2018;23:683-90.

NEUROANATOMIC, EPIGENETIC AND GENETIC DIFFERENCES IN MONOZYGOTIC TWINS DISCORDANT FOR ATTENTION DEFICIT HYPERACTIVITY DISORDER.

## Chen Y-C, Sudre G, Sharp W, et al.

The study of monozygotic twins discordant for attention deficit hyperactivity disorder can elucidate mechanisms that contribute to the disorder, which affects  $\Gamma$ ê+7% of children. First, using in vivo neuroanatomic imaging on 14 pairs of monozygotic twins (mean age 9.7, s.d. 1.9 years), we found that discordance for the disorder is mirrored by differing dimensions of deep brain structures (the striatum and cerebellum), but not the cerebral cortex. Next, using whole-blood DNA from the same twins, we found a significant enrichment of epigenetic differences in genes expressed in these 'discordant' brain structures. Specifically, there is differential methylation of probes lying in the shore and shelf and enhancer regions of striatal and cerebellar genes. Notably, gene sets pertaining to the cerebral cortex (which did not differ in volume between affected and unaffected twins) were not enriched by differentially methylated probes. Genotypic differences between the twin pairs - such as copy number and rare, single-nucleotide variants - did not contribute to phenotypic discordance. Pathway analyses of the genes implicated by the most differentially methylated probes implicated 3-aminobutyric acid (GABA), dopamine and serotonin neurotransmitter systems. The study illustrates how neuroimaging can help guide the search for epigenomic mechanisms in neurodevelopmental disorders

Monogr Soc Res Child Dev. 2016 Dec;81:96-110.

V. ELUCIDATING NEW PATHWAYS TO DIMENSIONS OF ADHD SYMPTOMS IN PRESCHOOL BY JOINTLY MODELING EXCUSIVE CONTROL AND FOUNDATIONAL COGNITIVE ABILITIES.

Nelson JM, James TD, Espy KA.

.....

Neuroimage Clin. 2017;15:376-82.

GENDER DIFFERENCES IN THE STRUCTURAL CONNECTOME OF THE TEENAGE BRAIN REVEALED BY GENERALIZED Q-SAMPLING MRI.

#### Tyan YS, Liao JR, Shen CY, et al.

The question of whether there are biological differences between male and female brains is a fraught one, and political positions and prior expectations seem to have a strong influence on the interpretation of scientific data in this field. This question is relevant to issues of gender differences in the prevalence of psychiatric conditions, including autism, attention deficit hyperactivity disorder (ADHD), Tourette's syndrome, schizophrenia, dyslexia, depression, and eating disorders. Understanding how gender influences vulnerability to these conditions is significant. Diffusion magnetic resonance imaging (dMRI) provides a noninvasive method to investigate brain microstructure and the integrity of anatomical connectivity. Generalized q-sampling imaging (GQI) has been proposed to characterize complicated fiber patterns and distinguish fiber orientations, providing an opportunity for more accurate, higher-order descriptions through the water diffusion process. Therefore, we aimed to investigate differences in the brain's structural network between teenage males and females using GQI. This study included 59 (i.e., 33 males and 26 females) age- and educationmatched subjects (age range: 13 to 14 years). The structural connectome was obtained by graph theoretical and network-based statistical (NBS) analyses. Our findings show that teenage male brains exhibit better intrahemispheric communication, and teenage female brains exhibit better interhemispheric communication. Our results also suggest that the network organization of teenage male brains is more local, more segregated, and more similar to small-world networks than teenage female brains. We conclude that the use of an MRI study with a GQI-based structural connectomic approach like ours presents novel insights into network-based systems of the brain and provides a new piece of the puzzle regarding gender differences

NeuroImage Clin. 2018;18:533-42.

**N**EURAL MECHANISMS UNDERLYING SUCCESSFUL AND DEFICIENT MULTI-COMPONENT BEHAVIOR IN EARLY ADOLESCENT **ADHD**.

.....

## Bluschke A, Gohil K, Petzold M, et al.

Attention Deficit Hyperactivity Disorder (ADHD) is a disorder affecting cognitive control. These functions are important to achieve goals when different actions need to be executed in close succession. This type of multicomponent behavior, which often further requires the processing of information from different modalities, is important for everyday activities. Yet, possible changes in neurophysiological mechanisms have not been investigated in adolescent ADHD. We examined N = 31 adolescent ADHD patients and N = 35 healthy controls (HC) in two Stop-Change experiments using either uni-modal or bi-modal stimuli to trigger stop and change processes. These stimuli were either presented together (SCD0) or in close succession of 300 milliseconds (SCD300). Using event-related potentials (ERP), EEG data decomposition and source localization we analyzed neural processes and functional neuroanatomical correlates of multicomponent behavior. Compared to HCs, ADHD patients had longer reaction times and higher error rates when Stop and Change stimuli were presented in close succession (SCD300), but not when presented together (SCD0). This effect was evident in the uni-modal and bi-modal experiment and is reflected by neurophysiological processes reflecting response selection mechanisms in the inferior parietal cortex (BA40). These processes were only detectable after accounting for intra-individual variability in neurophysiological data; i.e. there were no effects in standard ERPs. Multi-component behavior is not always deficient in ADHD. Rather, modulations in multi-component behavior depend on a critical temporal integration window during response selection which is associated with functioning of the inferior parietal cortex. This window is smaller than in HCs and independent of the complexity of sensory input

.....

NeuroImage Clin. 2018;18:744-52.

HEMISPHERIC BRAIN ASYMMETRY DIFFERENCES IN YOUTHS WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.

Douglas PK, Gutman B, Anderson A, et al.

**Introduction**: Attention-deficit hyperactive disorder (ADHD) is the most common neurodevelopmental disorder in children. Diagnosis is currently based on behavioral criteria, but magnetic resonance imaging (MRI) of the brain is increasingly used in ADHD research. To date however, MRI studies have provided mixed results in ADHD patients, particularly with respect to the laterality of findings.

**Methods**: We studied 849 children and adolescents (ages 6-21 y.o.) diagnosed with ADHD (n = 341) and age-matched typically developing (TD) controls with structural brain MRI. We calculated volumetric measures from 34 cortical and 14 non-cortical brain regions per hemisphere, and detailed shape morphometry of subcortical nuclei. Diffusion tensor imaging (DTI) data were collected for a subset of 104 subjects; from these, we calculated mean diffusivity and fractional anisotropy of white matter tracts. Group comparisons were made for within-hemisphere (right/left) and between hemisphere asymmetry indices (AI) for each measure. **Results**: DTI mean diffusivity AI group differences were significant in cingulum, inferior and superior longitudinal fasciculus, and cortico-spinal tracts (p < 0.001) with the effect of stimulant treatment tending to reduce these patterns of asymmetry differences. Gray matter volumes were more asymmetric in medication free ADHD individuals compared to TD in twelve cortical regions and two non-cortical volumes studied (p < 0.05). Morphometric analyses revealed that caudate, hippocampus, thalamus, and amygdala were more asymmetric (p < 0.0001) in ADHD individuals compared to TD, and that asymmetry differences were more significant than lateralized comparisons.

**Conclusions**: Brain asymmetry measures allow each individual to serve as their own control, diminishing variability between individuals and when pooling data across sites. Asymmetry group differences were more significant than lateralized comparisons between ADHD and TD subjects across morphometric, volumetric, and DTI comparisons

.....

Neuropsychiatr Dis Treat. 2018;14:581-85.

VITAMIN D AND VITAMIN D RECEPTOR LEVELS IN CHILDREN WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.

Sahin N, Altun H, Kurutas EB, et al.

**Objective**: In this study, we aimed to evaluate vitamin D and vitamin D receptor levels in children with attention-deficit/hyperactivity disorder (ADHD).

**Patients and methods**: In this cross-sectional study, a total of 80 children including 40 ADHD patients (aged 6-12 years; 28 males and 12 females) and 40 age-, sex-, and season of blood collection-matched controls (aged 6-12 years; 25 males and 15 females) were enrolled. Serum vitamin D and vitamin D receptor levels and calcium, phosphorus, and alkaline phosphatase were measured. The vitamin D receptor levels in the serum were measured using the quantitative sandwich enzyme immunoassay technique.

**Results**: Serum vitamin D and vitamin D receptor levels were found to be significantly lower in children with ADHD compared to healthy controls. No significant differences were found in serum calcium, phosphorus, and alkaline phosphatase levels. No significant differences were found among the ADHD subtypes in terms of serum vitamin D, vitamin D receptor, calcium, phosphorus and alkaline phosphatase levels.

**Conclusion**: This study suggests that children with ADHD have lower levels of vitamin D and vitamin D receptor. According to the authors knowledge, this is the first study to describe vitamin D receptor levels in ADHD

Neuropsychiatr Dis Treat. 2018;14:781-86.

CONTINUOUS PERFORMANCE TASK IN ADHD: IS REACTION TIME VARIABILITY A KEY MEASURE?

Llevy F, Pipingas A, Harris EV, et al.

**Objective**: To compare the use of the Continuous Performance Task (CPT) reaction time variability (intraindividual variability or standard deviation of reaction time), as a measure of vigilance in attention-deficit hyperactivity disorder (ADHD), and stimulant medication response, utilizing a simple CPT X-task vs an A-X-task.

**Method**: Comparative analyses of two separate X-task vs A-X-task data sets, and subgroup analyses of performance on and off medication were conducted.

**Results**: The CPT X-task reaction time variability had a direct relationship to ADHD clinician severity ratings, unlike the CPT A-X-task. Variability in X-task performance was reduced by medication compared with the children's unmedicated performance, but this effect did not reach significance. When the coefficient of variation was applied, severity measures and medication response were significant for the X-task, but not for the A-X-task.

**Conclusion**: The CPT-X-task is a useful clinical screening test for ADHD and medication response. In particular, reaction time variability is related to default mode interference. The A-X-task is less useful in this regard

.....

Neuropsychopharmacology, 2018:1-7.

A RANDOMIZED, PLACEBO-CONTROLLED TRIAL OF EXTENDED-RELEASE GUANFACINE IN CHILDREN WITH AUTISM SPECTRUM DISORDER AND ADHD SYMPTOMS: AN ANALYSIS OF SECONDARY OUTCOME MEASURES.

## Politte LC, Scahill L, Figueroa J, et al.

In a prior report, we showed that extended-release guanfacine (GEXR) is safe and effective for children with autism spectrum disorder (ASD) accompanied by ADHD symptoms. Here, we examine the impact of GEXR on oppositional behavior, anxiety, repetitive behavior, and sleep disturbance. Sixty-two subjects with ASD (53 boys, 9 girls; ages  $5\Gamma$ Cô14 years) were randomly assigned to GEXR (n = 30) or placebo (n = 32) for 8 weeks. Outcomes include the Home Situation Questionnaire-Modified for ASD (HSQ-ASD), Anxiety scale of the Child and Adolescent Symptom Inventory (CASI), Children CÖs Yale-Brown Obsessive-Compulsive Scale-Modified for ASD (CYBOCS-ASD), and ChildrenΓÇÖs Sleep Habits Questionnaire (CSHQ). A repeated measures linear mixed model was used to determine the effects of treatment group and time on HSQ scores. For other measures, change from baseline was evaluated with Analysis of Covariance (ANCOVA). After 8 weeks of treatment, parent ratings of oppositional behavior on the HSQ declined by 44% (per item mean from 3.4 to 1.9) in the GEXR group compared to 12% (from 3.3 to 2.9) for placebo (p = 0.004). Repetitive behavior on the CYBOCS-ASD showed a significantly greater decline in GEXR-treated participants compared to placebo (24% vs. <1%, p = 0.01). No group differences were observed on CASI Anxiety or CSHQ (p = 0.64 and 0.75, respectively), GEXR was effective in reducing oppositional behavior and, more modestly, repetitive behavior. GEXR was not superior to placebo for anxiety, though baseline anxiety ratings were low. GEXR did not significantly improve sleep habits. Future studies could focus on repetitive behavior or anxiety, symptoms with limited treatment options

.....

Neurosci Biobehav Rev. 2018 Mar;86:1-11.

PRENATAL ANTIDEPRESSANT EXPOSURE AND THE RISK OF ATTENTION-DEFICIT HYPERACTIVITY DISORDER IN CHILDREN: A SYSTEMATIC REVIEW AND META-ANALYSIS.

Man KKC, Chan EW, Ip P, et al.

This systematic review assesses the association between prenatal antidepressant exposure and risk of ADHD in children. Electronic databases were searched up to 25 July 2017. Observational studies examining this association were included in the review and meta-analysis was conducted where appropriate. Eight relevant studies were identified. The seven studies included in the meta-analysis comprised a total of 2,886,502 children. The pooled estimates comparing prenatal exposure to non-exposure showed an adjusted

rate ratio (aRR) of 1.39 (95%CI 1.21–1.61). Similarly, an increased risk was found comparing previous antidepressant users and non-users: aRR = 1.56 (95%CI 1.25–1.95). The relationship between maternal psychiatric conditions and ADHD in children yielded an aRR of 1.90 (95%CI 1.47–2.45). Three studies conducted sibling-matched analyses with aRR of 0.94 (95%CI 0.75–1.16). These data suggest that the observed association between prenatal use of antidepressants and risk of ADHD in offspring can be partially explained by confounding by indication because the results from sibling-matched analyses do not support an increased risk of ADHD in discordant exposed siblings

.....

Neurosci Biobehav Rev. 2018 Jan;84:63-71.

RISK OF UNINTENTIONAL INJURIES IN CHILDREN AND ADOLESCENTS WITH ADHD AND THE IMPACT OF ADHD MEDICATIONS: A SYSTEMATIC REVIEW AND META-ANALYSIS.

### Ruiz-Goikoetxea M, Cortese S, Aznarez-Sanado M, et al.

A systematic review with meta-analyses was performed to: 1) quantify the association between ADHD and risk of unintentional physical injuries in children/adolescents ('risk analysis'); 2) assess the effect of ADHD medications on this risk ('medication analysis'). We searched 114 databases through June 2017. For the risk analysis, studies reporting sex-controlled odds ratios (ORs) or hazard ratios (HRs) estimating the association between ADHD and injuries were combined. Pooled ORs (28 studies, 4,055,620 individuals without and 350,938 with ADHD) and HRs (4 studies, 901,891 individuals without and 20,363 with ADHD) were 1.53 (95% CI = 1.40,1.67) and 1.39 (95% CI = 1.06,1.83), respectively. For the medication analysis, we meta-analysed studies that avoided the confounding-by-indication bias [four studies with a self-controlled methodology and another comparing risk over time and groups (a 'difference in differences' methodology)]. The pooled effect size was 0.879 (95% CI = 0.838,0.922) (13,254 individuals with ADHD). ADHD is significantly associated with an increased risk of unintentional injuries and ADHD medications have a protective effect, at least in the short term, as indicated by self-controlled studies

.....

Neurosci Bull. 2018:1-10.

DOPAMINE D4 RECEPTOR GENE ASSOCIATED WITH THE FRONTAL-STRIATAL-CEREBELLAR LOOP IN CHILDREN WITH ADHD: A RESTING-STATE FMRI STUDY.

#### Qian A, Wang X, Liu H, et al.

Attention deficit hyperactivity disorder (ADHD) is a common childhood neuropsychiatric disorder that has been linked to the dopaminergic system. This study aimed to investigate the effects of regulation of the dopamine D4 receptor (DRD4) on functional brain activity during the resting state in ADHD children using the methods of regional homogeneity (ReHo) and functional connectivity (FC). Resting-state functional magnetic resonance imaging data were analyzed in 49 children with ADHD. All participants were classified as either carriers of the DRD4 4-repeat/4-repeat (4R/4R) allele (n = 30) or the DRD4 2-repeat (2R) allele (n = 19). The results showed that participants with the DRD4 2R allele had decreased ReHo bilaterally in the posterior lobes of the cerebellum, while ReHo was increased in the left angular gyrus. Compared with participants carrying the DRD4 4R/4R allele, those with the DRD4 2R allele showed decreased FC to the left angular gyrus in the left striatum, right inferior frontal gyrus, and bilateral lobes of the cerebellum. The increased FC regions included the left superior frontal gyrus, medial frontal gyrus, and rectus gyrus. These data suggest that the DRD4 polymorphisms are associated with localized brain activity and specific functional connections, including abnormality in the frontal-striatal-cerebellar loop. Our study not only enhances the understanding of the correlation between the cerebellar lobes and ADHD, but also provides an imaging basis for explaining the neural mechanisms underlying ADHD in children

Nord J Psychiatry. 2018;1-7.

NEURODEVELOPMENTAL DISORDERS: PREVALENCE AND COMORBIDITY IN CHILDREN REFERRED TO MENTAL HEALTH SERVICES.

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

**Background**: Accurate prevalence rates of the neurodevelopmental disorders (ND) and comorbid conditions in child and adolescent mental health services (CAMHS) are essential for treatment planning and organization of health care. However, valid and reliable prevalence estimates from Nordic CAMHS populations are scarce, and the published findings vary.

**Aims**: To report prevalence rates of ND (attention-deficit hyperactivity disorder: ADHD, tic disorder: TD or autism spectrum disorder: ASD) and comorbid disorders by a validated diagnostic instrument in children referred to CAMHS outpatient clinics.

**Methods**: Parents of 407 consecutively referred children aged 7-13-áyears were interviewed with the semistructured interview schedule for affective disorders and schizophrenia, present and lifetime version (Kiddie-SADS-PL) at time of admittance.

**Results**: One or more ND was diagnosed in 226 children (55.5%; 69.9% boys): ADHD (44.5%; 68.5% boys); TD (17.7%; 77.8% boys) and ASD (6.1%; 76% boys). Among children with ND 70 (31.0%) had only one ND with no comorbid disorder, 49 (21.7%) had more than one ND (homotypic comorbidity) and 131 (58%) had a non-ND psychiatric disorder (heterotypic comorbidity). Anxiety disorders were the most frequently occurring heterotypic comorbidity in all three ND. Comorbid depressive disorder was associated with older age, and comorbid anxiety disorder with female gender.

**Conclusion**: In children referred to CAMHS, ND constitute the most frequently occurring group of disorders, with high rates of both homotypic and heterotypic comorbidity. This needs to be taken into consideration in health service planning and treatment delivery

.....

Noropsikiyatr Ars. 2018;55:54-58.

EVALUATION OF THE RELATIONSHIP BETWEEN ATTENTION DEFICIT HYPERACTIVITY DISORDER SYMPTOMS AND CHRONOTYPE.

Tarakcioglu MC, Kadak MT, Akkin GG, et al.

**Introduction**: The aim of the study is to investigate the relationship between circadian characteristics and behavioral problems in children with Attention Deficit Hyperactivity Disorder (ADHD) (n=53), and to compare this group with healthy controls (n=38).

**Method**: Fifty-three medication-free children with ADHD, aged  $6\Gamma$ Çô12 years, and 38 healthy children, age and sex matched, participated. Parents completed the Conners $\Gamma$ ÇÖ Parent Rating Scale-Revised, the Children's Chronotype Questionnaire (CCTQ), and the Children  $\Gamma$ ÇÖs Sleep Habits Questionnaire (CSHQ) to assess sleep variables.

**Results**: ADHD children had more sleep-onset problems and parasomnias (in CSHQ) compared to healthy controls. However, circadian preferences did not differ between the groups in CCTQ scores. Another important finding was a mild correlation between parasomnia, bedtime on schooldays, and ADHD symptoms. **Conclusion**: Our study showed that children with ADHD showed more resistance to going to bed than did controls on school days. However, in contrast to our hypothesis, morningness/eveningness preference did not differ from controls in ADHD children

.....

Nutrition Research. 2018;52:39-47.

25-HYDROXVITAMIN D CONCENTRATIONS ARE NOT LOWER IN CHILDREN WITH BRONCHIAL ASTHMA, ATOPIC DERMATITIS, OBESITY, OR ATTENTION-DEFICIENT/HYPERACTIVITY DISORDER THAN IN HEALTHY CHILDREN.

Reinehr T, Langrock C, Hamelmann E, et al.

Vitamin D (vitD) is involved in immune regulation, and its receptor has been identified in several tissues including lung, adipose tissue, brain, and skin. Based on these observations, it has been suggested that vitD has an essential role not only in bone metabolism but also in other diseases such as atopic dermatitis (AD),

bronchial asthma (BA), attention-deficit/hyperactivity disorder (ADHD), and obesity because the affected tissues express vitD receptors. Furthermore, obesity, AD, and BA are regarded as inflammatory diseases. Therefore, we hypothesized that vitD concentrations are lower in children with AD, BA, ADHD, and obesity compared to healthy children. We measured 25-hydroxyvitamin D concentrations in 235 children (60% boys, age 9.3±1.7years) with obesity, BA, AD, or ADHD and compared them to those of 3352 children from a healthy population. Additionally, parathyroid hormone was measured in the children with obesity, ADHD, BA, and AD compared to healthy children. In multiple regression analyses adjusted to migration background, time period of blood sample, age, and sex, VitD levels correlated significantly with the severity of AD measured by SCORing Atopic Dermatitis index and attention deficit measured by Conners questionnaire in ADHD. VitD levels were not linked to hyperactivity in ADHD, the severity of BA measured as forced expiration volume in the first second, or body mass index standard deviation score. Parathyroid hormone was not associated with the activity of any analyzed disease. In conclusion, most of our findings do not support the hypothesis that vitD is involved in the pathogenesis of these entities

.....

Nutritional Neuroscience. 2018;1-14.

EVALUATION OF DIETARY INTAKE IN CHILDREN AND COLLEGE STUDENTS WITH AND WITHOUT ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.

Holton KF, Johnstone JM, Brandley ET, et al.

**OBJECTIVES**: To evaluate dietary intake among individuals with and without attention-deficit hyperactivity disorder (ADHD), to evaluate the likelihood that those with ADHD have inadequate intakes.

**METHODS**: Children, 7-12 years old, with (n = 23) and without (n = 22) ADHD, and college students, 18-25 years old, with (n = 21) and without (n = 30) ADHD comprised the samples. Children's dietary intake was assessed by a registered dietitian using 24-hour recalls over 3 days. College students kept a detailed food record over three days. Dietary information for both groups was entered into the Nutrition Data Systems for Research database, and output was analyzed using SAS 9.4. Nutrient analyses included the Healthy Eating Index-2010, Micronutrient Index (as a measure of overall micronutrient intake), and individual amino acids necessary for neurotransmission. Logistic regression was used to model the association of nutrient intake with ADHD. Models were adjusted for age, sex, IQ (or GPA), and energy intake (or total protein intake) as appropriate. Significance was evaluated at P = 0.05, and using the Benjamini-Hochberg corrected P-value for multiple comparisons.

**RESULTS**: No evidence existed for reduced nutrient intake among those with ADHD compared to controls in either age group. Across both groups, inadequate intakes of vitamin D and potassium were reported in 95% of participants. Children largely met nutrient intake guidelines, while college students failed to meet these guidelines for nine nutrients. In regards to amino acid intake in children, an increased likelihood of having ADHD was associated with higher consumption of aspartate,  $OR = 12.61 \ (P = 0.01)$  and glycine  $OR = 11.60 \ (P = 0.05)$ ; and a reduced likelihood of ADHD with higher intakes of glutamate,  $OR = 0.34 \ (P = 0.03)$ . Among young adults, none of the amino acids were significantly associated with ADHD, though glycine and tryptophan approached significance.

**DISCUSSION**: Results fail to support the hypothesis that ADHD is driven solely by dietary micronutrient inadequacy. However, amino acids associated with neurotransmission, specifically those affecting glutamatergic neurotransmission, differed by ADHD status in children. Amino acids did not reliably vary among college students. Future larger scale studies are needed to further examine whether or not dietary intake of amino acids may be a modulating factor in ADHD

OMICS, 2017 Jun:21:352-58.

REGULATING THE REGULATORS IN ATTENTION-DEFICIT/HYPERACTIVITY DISORDER: A GENETIC ASSOCIATION STUDY OF MICRORNA BIOGENESIS PATHWAYS.

#### Karakas U, Ay OI, Ay ME, et al.

Attention-deficit/hyperactivity disorder (ADHD) is one of the most prevalent complex psychiatric disorders in children as well as adults. ADHD impacts not only the affected individuals but also their families and social and professional networks. The clinical and diagnostic criteria for ADHD remain imprecise, in part, due to lack of robust biomarkers. ADHD comprises multiple subsets of diseases that present a shared set of downstream clinical findings, while displaying extensive molecular heterogeneity. This calls for innovation in diagnostic strategies that can help establish an ADHD diagnosis unequivocally as well as guiding precision medicine in this common mental health disorder. No study has examined, to the best of our knowledge, the upstream regulation of miRNAs that impact the downstream final ADHD phenotype. The latter focus on putative genetic biomarkers that regulate the regulators and can be tested empirically, for example, through genetic association analyses of the biogenesis pathways for miRNAs that impact the ADHD phenotype. Hence, we report here polymorphic variation in 10 miRNA biogenesis pathway candidate genes, including RNASEN, DGCR8, XPO5, RAN, DICER1, TARBP2, AGO1, AGO2, GEMIN3, and GEMIN4, in a large sample from the Eastern Mediterranean region (N = 355; 191 cases and 164 controls). We found that AGO1 rs595961 was significantly associated with ADHD susceptibility (p < 0.05). While polymorphic variation in other miRNA biogenesis pathway genes did not display a significant association in the present sample, the observations reported herein on miRNA biogenesis variation offer a new avenue of research for innovation in biomarker discovery concerning ADHD and other complex psychiatric diseases with major global health burden

.....

Osteoporos Int. 2016 Jul;27:2223-27.

MEDICATION THERAPY FOR ATTENTION DEFICIT/HYPERACTIVITY DISORDER IS ASSOCIATED WITH LOWER RISK OF FRACTURE: A RETROSPECTIVE COHORT STUDY.

Perry BA, Archer KR, Song Y, et al.

**UNLABELLED**: The impact of pharmacotherapy for attention deficit/hyperactivity disorder on fracture risk has not been well studied. In this retrospective cohort study, medication therapy was associated with lower fracture incidence. Further studies are needed to better characterize the short-term and long-term effects of these medications on bone health and fracture risk.

**INTRODUCTION**: Attention deficit/hyperactivity disorder (ADHD) is associated with increased risk of bone fractures. The impact of pharmacotherapy with either stimulant or non-stimulant medications on fracture risk has not been well characterized. We performed a study to compare fracture incidence in ADHD patients treated with stimulant or non-stimulant medications vs. no pharmacotherapy.

**METHODS**: In this retrospective cohort study, data were extracted from a large electronic medical record. A total of 10,066 subjects with ADHD, 40 years or younger, were included. We extracted data regarding stimulant and non-stimulant ADHD medications, corticosteroids, fracture data, demographic data, and diabetes history.

**RESULTS**: A total of 1015 patients (10 %) sustained fractures. Multivariable Cox proportional hazard analysis indicated that compared to those with two or more prescriptions for an ADHD medication, individuals without documented medication therapy had a significantly increased hazard of fracture (hazard ratio [HR] 3.9, 95 % confidence interval [CI] 2.6-5.9). However, the hazard ratio for stimulant vs. non-stimulant medication (HR 0.92, 95 % CI 0.60-1.4) was not statistically significant.

**CONCLUSIONS**: Three times as many patients with no documented ADHD medication prescriptions suffer a fracture compared to patients with a history of two or more prescriptions for an ADHD medication. Treatment and adherence are thus important to prevent fracture in this population

Pediatr Diabetes, 2018.

PREVIOUSLY UNDIAGNOSED ATTENTION-DEFICIT/HYPERACTIVITY DISORDER ASSOCIATED WITH POOR METABOLIC CONTROL IN ADOLESCENTS WITH TYPE 1 DIABETES.

Nylander C, Lindstr+Âm K, Khalifa N, et al.

**Background**: Managing modern diabetes treatment requires efficient executive functions. Patients with attention-deficit/hyperactivity disorder (ADHD) and type 1 diabetes have poor metabolic control and present with ketoacidosis more often than patients without ADHD.

**Objective**: To assess whether patients with type 1 diabetes and with indications of executive problems met criteria for ADHD, and to investigate whether these patients had difficulties achieving metabolic control. Methods: In a hospital-based study, including 3 pediatric departments at hospitals in Stockholm and Uppsala, Sweden, questionnaires regarding executive problems had been filled out by 12- to 18-year-old patients with type 1 diabetes and their parents. Out of 166 patients with completed questionnaires, 49 were selected for a clinical study due to reported executive problems/ADHD symptoms. However, 7 already had a diagnosis of ADHD, 21 denied follow-up, 8 did not respond, leaving 13 adolescents for the clinical assessment.

**Results**: Of the clinically assessed adolescents, 9 (6 girls) met criteria for ADHD. Patients who did not respond to the follow-up and patients who were diagnosed with ADHD within the study, showed to a larger extent than the other study groups high HbA1c levels (>70mmol/mol, 8,6%). HbA1c >70mmol/mol (8.6%) was associated with diagnosed ADHD (prior to or within the study), odds ratio 2.96 (95% confidence interval 1.02-8.60).

**Conclusion**: Patients with type 1 diabetes and poor metabolic control should be assessed with regard to ADHD. There is a need for paying special attention to girls with poor metabolic control

.....

Pediatr Int. 2018;60:247-53.

ALEXITHYMIA, DEPRESSION AND ANXIETY IN PARENTS OF CHILDREN WITH NEURODEVELOPMENTAL DISORDER: COMPARATIVE STUDY OF AUTISTIC DISORDER, PERVASIVE DEVELOPMENTAL DISORDER NOT OTHERWISE SPECIFIED AND ATTENTION DEFICIT-HYPERACTIVITY DISORDER.

Durukan, Kara K, Almbaideen M, et al.

**Background**: Recent studies have shown that individuals with neurodevelopmental disorders and their relatives have problems expressing and recognizing emotions, but there is a lack of studies on alexithymia, and the relationship between parental alexithymia and depression anxiety symptoms in these groups. The aim of this study was therefore to measure alexithymia, depression, and anxiety levels in parents of children with pervasive developmental disorders and attention deficit hyperactivity disorder (ADHD), and determine whether there is a positive correlation between the child's neurodevelopmental problem severity and parent scores.

**Methods**: Parents of 29 autistic disorder (AD), 28 pervasive developmental disorder not otherwise specified (PDD-NOS) and 29 ADHD children were recruited into the study, and completed a demographic information form, as well as the Toronto Alexithymia Scale (TAS-20), Beck Depression Inventory, and State Trait Anxiety Inventory.

Results: Alexithymia symptoms were higher in parents of children with AD than in others but unexpectedly, also these symptoms were higher in ADHD parents than in PDD-NOS groups. In addition, there were unexpected differences according to alexithymia subtype, while only the difference in maternal TAS-1 scores (difficulty in describing feelings) were statistically significant. Parental depression and state anxiety scores were increased as the child's symptom severity increased, but trait anxiety symptoms were higher in the AD and ADHD group than in the PDD-NOS group. In all groups, maternal depression and anxiety scores were higher than paternal scores, and differences were significant for depression and anxiety types in AD, and for only anxiety types in ADHD parents. The AD group had the strongest correlation between parental depression anxiety and alexithymia.

**Conclusion**: The possibility of alexithymia, depression and anxiety should be kept in mind when working with parents of children with neurodevelopmental disorders

PLoS ONE. 2018;13.

MEDICATION CHANGES AFTER SWITCHING FROM CONCERTA-« BRAND METHYLPHENIDATE HCL TO A GENERIC LONG-ACTING FORMULATION: A RETROSPECTIVE DATABASE STUDY.

#### Fife D, Cepeda MS, Baseman A, et al.

**Background** Observational studies of switching from branded to generic formulations of the same drug substance often lack appropriate comparators for the subjects who switched. Three generic formulations were deemed equivalent to Concerta: an authorized generic (AG) identical except for external packaging, and two other generics (EG).

**Objective** Compare the incidence of a combined endpoint (switching back to Concerta, changing the use of immediate release methylphenidate (MPH), stopping all long-acting methylphenidate, or starting a new medication) among people switched from Concerta to the AG versus the EG.

**Methods** Cohort study from the Truven CCAE database of people aged 6 to 65 diagnosed with ADHD, treated with Concerta, and switched to the EG or to the AG formulation.

**Results** In the EG arm 24.6% and in the AG arm 19.7% of subjects switched back to Concerta. The proportion of subjects meeting the combined endpoint was 39.5% in the EG arm, 32.9% in the AG arm, a crude risk ratio of 1.20 (95% CI 0.94, 1.54). After adjustment by propensity score stratification, the adjusted odds ratio (OR) was 1.23 (95% CI 0.90, 1.70). In an unplanned analysis using a different method of adjustment, the adjusted OR was 1.00 (95% CI 0.69, 1.44).

**Discussion** This study did not detect a difference between the proportion of people who met the study endpoint in the two study arms, i.e. between those who switched to a generic formulation that was identical to Concerta except for external packaging and those who switched to the comparison generics. The high incidence of the combined endpoint in the AG arm demonstrates the need for an appropriate comparator in studies of this type

.....

Prog Neuro-Psychopharmacol Biol Psychiatry. 2018;84:122-28.

ASSOCIATION ANALYSIS OF NOREPINEPHRINE TRANSPORTER POLYMORPHISMS AND METHYLPHENIDATE RESPONSE IN ADHD PATIENTS.

#### Angyal N, Horvath EZ, Tarnok Z, et al.

**Aims**: Methylphenidate (MPH) is the most frequently prescribed drug in Attention Deficit Hyperactivity Disorder (ADHD). Hitherto mostly the dopamine transporter gene has been studied in MPH-response and only a few studies analyzed the norepinephrine transporter (NET, SLC6A2) gene, although MPH is a potent inhibitor of both dopamine and norepinephrine transporters. We aimed to analyze this monoamine transporter gene in relation to ADHD per se and MPH-response in particular to gain further knowledge in ADHD pharmacogenetics using a Caucasian sample.

**Methods**: Six single nucleotide polymorphisms (rs28386840, rs2242446, rs3785143, rs3785157, rs5569, rs7194256 SNP) were studied across the NET gene in 163 ADHD children (age:  $9.3 \pm 2.6$ ; 86.5% male) using ADHD-RS hyperactivity-impulsivity and inattention scales. For case-control analysis 486 control subjects were also genotyped. At the MPH-response analysis responders had minimum 25% decrease of ADHD-RS total score after 2 months of treatment, and chi-square test compared 90 responders and 32 non-responders, whereas ANOVA was used to assess symptom improvement after the first month among the 122 ADHD patients.

**Results**: The classical case-control analysis did not yield any association with ADHD diagnosis, which was supported by meta-analysis conducted on the available genetic data (combining previously published and the present studies). On the other hand, the intronic rs3785143 showed nominal association with inattention symptoms (p = 0.01). The haplotype analysis supported this association, and indicated the importance of the first haploblock encompassing the intronic and 2 promoter SNPs. With MPH-response only the promoter rs28386840 showed nominal association: Those with at least one T-allele were overrepresented in the responder group (42% vs 19%, p = 0.08), and they had better improvement on the hyperactivity-impulsivity scale compared to the AA genotype (p = 0.04).

**Conclusion**: Although none of our single SNP findings remained significant after correcting for multiple testing, our results from the MPH-response analysis indicate the potential importance of promoter variants in the NET gene

.....

Psiquiatr Biol. 2018.

THE CHALLENGE OF THE COMORBID DIAGNOSIS IN CHILDHOOD AND ADOLESCENT PSYCHIATRY.

González SC, Geijo US, Mongil LpB, et al.

The case is presented of a patient with a changing behavioural phenotype and a rare biotype, who was diagnosed with attention deficit hyperactivity disorder (ADHD) from an early age, with partial response to the prescribed treatment (extended-release methylphenidate, risperidone, sertraline). After an aggressive episode at home, he was admitted to the child and adolescent hospitalisation unit. A brain NMR scan and a metabolic study revealed anomalies compatible with a deficiency of ornithine transcarbamylase (OTC), an enzyme which forms part of the urea cycle. The study discusses the different diagnoses that were proposed given the syndrome of the patient, both from an organic approach, as well as and from the perspective of psychiatric comorbidity. OTC deficiency has a low incidence -one in every 15,000 newborn babies-, similar to that of phenylketonuria (which was included years ago in the newborn screening program in Spain). This is a predominantly hereditary disease (X-linked transmission), but with several described cases of de novo mutations or deletions. Complete OTC deficiency shows its symptoms in the first years of life, whereas a partial deficiency could start during late childhood or even in adolescence, with unspecific neuropsychiatric or behavioural symptoms. A clear pattern has not been established

.....

Psychiatr Serv. 2018;69:322-31.

RACIAL-ETHNIC DIFFERENCES IN PATTERNS OF DISCONTINUOUS MEDICATION TREATMENT AMONG MEDICAID-INSURED YOUTHS WITH ADHD.

Ji X, Druss BG, Lally C, et al.

**Objective**: This study examined the association between race-ethnicity and patterns of medication gaps and discontinuities among Medicaid-insured children initiating pharmacotherapy for attention-deficit hyperactivity disorder (ADHD).

**Methods**: Medicaid claims data from nine states were used to identify racial-ethnic differences in patterns of ADHD medication treatment among 102,669 children initiating ADHD medication. Multinomial logistic regression with state indicators was used to estimate these differences, with adjustment for individual and contextual confounders.

**Results**: Approximately three-fifths of the sample did not receive continuous medication treatment as defined by HEDIS guidelines; among them, one-fifth discontinued treatmentwith no subsequent reinitiation (early termination), less than onetenth reinitiated pharmacotherapy following a single medication gap, more than three-Tenths experienced discontinuous pharmacotherapy with two gaps, and more than four-Tenths experienced discontinuous pharmacotherapy with three or more gaps. Compared with white children, black children had a 25% relative increase in the likelihood of early termination andHispanic children had a 21% relative increase (p,.001); their relative increases in the likelihood of twomedication gapswere 41% and 29%, respectively (p,.001), and for three ormore gaps they were 56% and 40%, respectively (p,.001).

**Conclusions**: Black and Hispanic children were much more likely than white children to be classified as discontinuing ADHD medication treatment, according to HEDIS. The differences predominantly occurred because youths from minority groups were more likely to experience multiple medication gaps, rather than complete discontinuation. Future studies should examine reasons for these multiple gaps to inform interventions to improve ADHD treatment continuity

Psychiatriki. 2017 Jan;28:28-36.

ATTENTION DEFICIT/HYPERACTIVITY DISORDER (ADHD) SYMPTOMS AND COGNITIVE SKILLS OF PRESCHOOL CHILDREN.

#### Thomaidis L, Choleva A, Janikian M, et al.

Attention deficit/hyperactivity disorder (ADHD) constitutes a neurobehavioral disorder which may potentially adversely affect children's wellbeing and academic achievement. The onset of symptoms is present prior to 12 years of age, and often the symptoms are evident in the preschool years. In fact, it has been suggested that screening for ADHD symptoms may be initiated as early as four years of age. Preschool children with ADHD have been shown to present with poor pre-academic skills and might be at increased risk for numerous school-related problems, including functional impairment during elementary school years and persistent poor academic performance thereafter. Although preschool years are characterized by rapid cognitive growth, preschoolers with ADHD may present with poorer cognitive and neuropsychological functioning. Due to the early onset of ADHD symptoms, exploring the cognitive correlates of this condition among preschool children is thought to be of notable importance. The aim of the present study was to evaluate any association between ADHD symptoms and cognitive skills among preschool children. A cross-sectional study was conducted among a nationwide random sample of 4,480 preschool children. ADHD symptoms were assessed though interviews with parents and teachers based on DSM-IV-TR criteria. Cognitive skills were assessed through a standardized school readiness test (A' TEST). Among participants, the occurrence of ADHD symptoms was 4.6% (boys/girls: 3.4/1). The presence of ADHD symptoms among children was inversely associated with non-verbal and verbal cognitive skills; specifically, with abstract thinking (aOR 1.97, 95% CI 1.30-3.00), language (2.36, 1.55-3.59), critical reasoning (2.58, 1.84-3.62), visual perception (2.42, 1.38-4.24), and visual motor skills (2.61, 1.91-3.55). Children with ADHD symptoms were five times as likely to have compromised organizational skills (4.92, 3.04-7.97). Abstract thinking was the least affected domain particularly among boys, while organizational skills were the most affected domain in both sexes, and possibly more among girls. Concluding, the present study confirms that even during preschool years, children with ADHD symptoms are more likely to present with concomitant cognitive difficulties. Thus, screening for the presence of ADHD, as well as cognitive and affective screenings among preschool aged children may facilitate the early detection and determent of the development of cognitive difficulties, and subsequently the early intervention for fostering skills that are amenable to change, such as organizational skills and planning. As a result, the study findings reveal the necessity for the evaluation of pre-academic skills among preschool children with ADHD symptoms in order to mitigate unfavorable academic functioning

Psychiatr Invest. 2018:15:13-23.

DEVELOPING THE SYMPTOMS AND FUNCTIONAL IMPAIRMENT RATING SCALE: A MULTI-DIMENSIONAL ADHD SCALE. Du Y, Li M, Jiang W, et al.

.....

**Objective** This research developed a practical, multi-dimensional attention deficit hyperactivity disorder (ADHD) rating scale (i.e., the Symptoms and Functional Impairment Rating Scale, SFIRS) for Chinese children, aged 6–12 years, with ADHD.

**Methods** The structural validity, criterion validity, internal consistency, and test-retest reliability of the scale were evaluated. Item screening was conducted with 412 ADHD patients and 322 developmentally typical controls.

**Results** The scale includes 44 items, divided among Hyperactivity-Impulsivity, Self-Control, Inattention, Self-Management, Academic Performance, and Social Interaction. The six-factor model showed good data fit, with each factor significantly correlated with its corresponding criterion (r=0.690-0.841). The Cronbach's  $\alpha$  of the full scale was 0.976. Total score test-retest reliability was r=0.816 (p<0.01).

**Conclusion** The SFIRS thus demonstrated good reliability and validity and may be used to assess ADHD among children aged 6–12 years in China.

Newsletter – ADHD marzo 2018

Psychiatr Invest. 2018;15:172-77.

COMPARATIVE ANALYSIS OF THE WISC BETWEEN TWO ADHD SUBGROUPS.

Kubo Y, Kanazawa T, Kawabata Y, et al.

**Objective** The prevalence of attention deficit/hyperactivity disorder (ADHD) in school-age children is 7.2%, and ADHD is divided into clinical subtypes.

**Methods** The current study explored whether specific cognitive profiles as assessed using the Wechsler Intelligence Scale for Children (WISC)-IV could be obtained for each clinical ADHD subtype (ADHD-Inattentive type and ADHD-Combined type) and investigated the correlation between WISC scores and parental age at their children ΓÇÖs birth or birthweight. The enrolled sample comprised 12 AD-HD-I and 15 ADHD-C subjects.

**Results** An impaired Processing Speed Index was found in ADHD-I. The age of the father at the child's birth and birthweight positively correlated with the full scale intelligence quotient (FSIQ) score in the WISC assessment.

**Conclusion** Inattentiveness within the behaviors of the children with ADHD-I is partly due to the impaired processing speed, therefore effective support for ADHD will be conducted if educator decreases their speaking speed. Since biological basis of ADHD is still largely unknown, future studies using both psychological and biological methods will reveal the etiology of ADHD. These scientific assessments will provide information for more effective approaches in the care of children with ADHD

.....

Psychiatr Invest. 2018;15:90-93.

TREATMENT OF CHILDREN AND ADOLESCENTS WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER AND/OR TOURETTE'S DISORDER WITH CLONIDINE EXTENDED RELEASE.

#### Joo SW, Kim H-W.

We aimed to assess the effectiveness and safety of clonidine extended release (ER) treatment in Korean youth with ADHD and/or Tourette $\Gamma$ ÇÖs disorder. We retrospectively reviewed the medical records of 29 children and adolescents treated with clonidine ER. The effectiveness were retrospectively measured at baseline and after 4 and 12 weeks based on the Clinical Global Impression-Severity (CGI-S) and Clinical Global Impression-Improvement (CGI-I) scores. Safety was evaluated at each visit based on spontaneous reports from the subjects or from their parents/guardians. Significant decreases in the CGI-S scores for both ADHD (F=23.478, p<0.001, partial + $\lambda$ 2=0.540) and tic symptoms (F=15.137, p<0.001, partial + $\lambda$ 2=0.443) were noted over 12 weeks. The most common adverse event was somnolence (n=9, 31.0%) and lifethreatening adverse effects were not observed. Our results provide preliminary evidence for the effectiveness and safety of clonidine ER

Psychol Med. 2017 Jul;47:1771-83.

ADHD PATIENTS FAIL TO MAINTAIN TASK GOALS IN FACE OF SUBLIMINALLY AND CONSCIOUSLY INDUCED COGNITIVE CONFLICTS.

#### Gohil K, Bluschke A, Roessner V, et al.

**BACKGROUND**: Attention deficit hyperactivity disorder (ADHD) patients have been reported to display deficits in action control processes. While it is known that subliminally and consciously induced conflicts interact and conjointly modulate action control in healthy subjects, this has never been investigated for ADHD.

**METHOD**: We investigated the (potential) interaction of subliminally and consciously triggered response conflicts in children with ADHD and matched healthy controls using neuropsychological methods (event-related potentials; ERPs) to identify the involved cognitive sub-processes.

**RESULTS**: Unlike healthy controls, ADHD patients showed no interaction of subliminally and consciously triggered response conflicts. Instead, they only showed additive effects as their behavioural performance (accuracy) was equally impaired by each conflict and they showed no signs of task-goal shielding even in cases of low conflict load. Of note, this difference between ADHD and controls was not rooted in early bottom-up attentional stimulus processing as reflected by the P1 and N1 ERPs. Instead, ADHD showed either no or reversed modulations of conflict-related processes and response selection as reflected by the N2 and P3 ERPs.

**CONCLUSION**: There are fundamental differences in the architecture of cognitive control which might be of use for future diagnostic procedures. Unlike healthy controls, ADHD patients do not seem to be endowed with a threshold which allows them to maintain high behavioural performance in the face of low conflict load. ADHD patients seem to lack sufficient top-down attentional resources to maintain correct response selection in the face of conflicts by shielding the response selection process from response tendencies evoked by any kind of distractor

.....

Psychoneuroendocrinology. 2017 Jul;81:29-35.

MATERNAL HYPOTHYROXINAEMIA IN EARLY PREGNANCY AND PROBLEM BEHAVIOR IN 5-YEAR-OLD OFFSPRING.

Oostenbroek MHW, Kersten RHJ, Tros B, et al.

**INTRODUCTION**: There is evidence, though not consistent, that offspring born to mothers with subtle decreases in thyroid function early in their pregnancies may be at risk of cognitive impairments and attention problems. However, other types of problem behavior have not been addressed thus far. We tested whether maternal thyroid function in early pregnancy is associated with several types of problem behavior in offspring at age 5-6 years.

**METHODS**: This was a longitudinal study that included the data of 2000 mother-child pairs from the Amsterdam Born Children and their Development study. At a median gestational age of 12.9 (interquartile range: 11.9-14.1) weeks, maternal blood was sampled for assessment of free T4 and TSH. Overall problem behavior, hyperactivity/inattention, conduct problems, emotional problems, peer relationship problems and prosocial behavior were measured at age 5-6 years using the Strengths and Difficulties Questionnaire, which was filled out by both parents and teachers.

**RESULTS**: Maternal hypothyroxinaemia <5th percentile was associated with a 1.70 (95% confidence interval (CI): 1.01-2.86) increased odds of teacher-reported hyperactivity/inattention after adjustment for confounders. By increasing the cut-off level to <10th percentile, the odds ratio became 1.47 (95% CI: 0.99-2.20). There were no associations between maternal thyroid function parameters and hyperactivity/inattention as reported by parents, nor with teacher or parent reports of other types of problem behavior.

**CONCLUSIONS**: Our results partially confirm previous observations, showing that early disruptions in the maternal thyroid hormone supply may be associated with ADHD symptoms in offspring. Our study adds that there is no evidence for an effect on other types of problem behavior

.....

Psychoneuroendocrinology. 2018;90:174-81.

SALIVARY CORTISOL AND ALPHA-AMYLASE DIURNAL PROFILES AND STRESS REACTIVITY IN CHILDREN WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER.

Angeli E, Korpa T, Johnson EO, et al.

There is growing evidence for dysregulation of the stress system in individuals with Attention Deficit Hyperactivity Disorder (ADHD). The stress system includes neuroanatomical and functional components that function in concert to maintain homeostasis and its main effectors are the hypothalamic-pituitary-adrenal (HPA) axis and the sympathetic/adrenomedullary nervous system (SNS). As stress system activity demonstrates a distinct circadian variation, we aimed to describe simultaneously, diurnal rhythms of both the HPA axis and the SNS in children with ADHD and a comparison group. Moreover, we attempted to investigate stress responses to a physical stressor, venipuncture, in both groups. Sixty-two prepubertal children with ADHD combined (ADHD-C) or inattentive (ADHD-I) type and 40 typically developing children provided saliva samples at six specific time points during a day, as well as before and 10 min after a scheduled morning venipuncture. Salivary cortisol and +!- amylase were selected as reliable noninvasive biomarkers for HPA axis and SNS function and were measured in the samples obtained. Results revealed that children with ADHD-C had lower mean cortisol values both 30 min after awakening and at 18:00 h than controls (p = 0.002 and p = 0.018 respectively), as well as lower mean Cortisol Awakening Response (CAR) and Area Under the Curve for wake to bed period (AUCi) values of cortisol (p = 0.004 and p = 0.001, respectively). Also,

mean CAR and cortisol AUCi were lower in children with ADHD-I than the control group (p = 0.034 and p = 0.038 respectively). Alpha-amylase measurements showed an increase over time (p < 0.001), which was similar in all three groups. Interestingly, +!-amylase changes over time were correlated with the corresponding cortisol changes (p < 0.001). Venipuncture, elicited a significant increase only in +!-amylase levels and more so in the control group (p = 0.003). These findings suggest a partial hypofunction of the stress system in children with ADHD

.....

Rev Neurol. 2017 Feb;64:S101-S104.

ATTENTION DEFICIT HYPERACTIVITY DISORDER: FROM A NEURODEVELOPMENTAL PERSPECTIVE.

Fernandez-Jaen A, Lopez-Martin S, Albert J, et al.

**INTRODUCTION**: Neurodevelopmental disorders cover a heterogeneous group of disorders such as intellectual disability, autism spectrum disorders or specific learning difficulties, among others. The neurobiological and clinical variables seem to clearly justify the recent inclusion of attention deficit hyperactivity disorder (ADHD) as a neurodevelopmental disorder in the international classifications.

**DEVELOPMENT**: Neurodevelopmental disorders are characterised by their dimensional nature and the distribution of the different symptoms in the population. These aspects are reviewed, specifically from the perspective of the clinical features and the neuropsychology of ADHD. The dimensional symptomatic nature of ADHD contrasts with the diagnostic criteria of this disorder according to different classifications or clinical guidelines. It also contrasts with the data collected by means of different complementary examinations (scales, tests, etc.).

**CONCLUSIONS**: It is essential to understand the clinical continuum within each neurodevelopmental disorder (including ADHD), among the different neurodevelopmental disorders, and among the neurodevelopmental disorders and normality for their research, diagnosis and management. The development of instruments that provide support for this dimensional component is equally significant

Rev Neurol. 2017 Feb:64:S65-S72.

NEUROPSYCHOLOGY OF TOURETTE'S DISORDER: COGNITION, NEUROIMAGING AND CREATIVITY.

Espert R, Gadea M, Alino M, et al.

**INTRODUCTION**: Tourette's disorder is the result of fronto-striatal brain dysfunction affecting people of all ages, with a debut in early childhood and continuing into adolescence and adulthood.

**DEVELOPMENT**: This article reviews the main cognitive, functional neuroimaging and creativity-related studies in a disorder characterized by an excess of dopamine in the brain.

**CONCLUSIONS**: Given the special cerebral configuration of these patients, neuropsychological alterations, especially in executive functions, should be expected. However, the findings are inconclusive and are conditioned by factors such as comorbidity with attention deficit hyperactivity disorder and obsessive-compulsive disorder, age or methodological variables. On the other hand, the neuroimaging studies carried out over the last decade have been able to explain the clinical symptoms of Tourette's disorder patients, with special relevance for the supplementary motor area and the anterior cingulate gyrus. Finally, although there is no linear relationship between excess of dopamine and creativity, the scientific literature emphasizes an association between Tourette's disorder and musical creativity, which could be translated into intervention programs based on music

.....

Rev Neurol. 2017 Feb;64:S59-S63.

**LEARNING DISORDERS IN NEUROFIBROMATOSIS TYPE 1.** 

Garcia-Penas JJ.

**INTRODUCTION**: Neurocognitive deficits and academic learning difficulties are the most common neurologic complication of neurofibromatosis type 1 (NF1) in childhood and can be responsible for significant lifetime

morbidity. Children with NF1 show impairments in attention, visual perception, language, executive function, academic skills, and behavior. Studies in animal models suggest that the learning disabilities associated with NF1 are caused by excessive Ras activity that leads to increased gamma-aminobutyric acid (GABA) inhibition and to decreased long-term potentiation. AIM: To describe the frequency, severity, typology, and natural course of specific cognitive deficits in children with NF1.

**DEVELOPMENT**: Cognitive and behavioral disorders affect between 50-80% of all children with NF1. We can define three subtypes of cognitive profiles in children with NF1 and learning disorder, including global learning disorder, specific learning disorder, and isolated attention deficit hyperactivity disorder. The most common cognitive deficits are connected with visual-spatial impairment, however working memory and executive function deficits associated with prefrontal cortex dysfunction are also important.

**CONCLUSIONS**: There is an extremely high frequency of cognitive problems in children with NF1, making cognitive dysfunction the most common complication to affect quality of life in these children. Early diagnosis and treatment of learning disorders in these patients leads to improved academic outcome

.....

Rev Neurol. 2017 Feb;64:S3-S7.

TREATMENTS FOR CHILDREN AND ADOLESCENTS WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER: WHAT IS THE EVIDENCE BASE TO DATE?

#### Cortese S, Rosello-Miranda R.

The evidence base from empirical studies is one of the elements, along with patients' preference and consideration of particular clinical state and circumstances, that should be taken into account in the process of clinical decision making. This paper provides an overview of the current evidence base for the treatment of attention-deficit-hyperactivity disorder (ADHD), drawing on the results of the most recent meta-analyses of randomized controlled trials assessing the pharmacological and non-pharmacological treatment of ADHD. Overall, available recent meta-analyses show that psychostimulants, and, although to a less extent, non psychostimulants, are efficacious in terms of control of core ADHD symptoms, at least in the short term; and although the efficacy of non-pharmacological treatments (behavioral interventions, diet, cognitive training and neurofeedback) for ADHD core symptoms remains uncertain, some non-pharmacological approach are efficacious for ADHD-related problems, such as behavioral interventions for oppositional problems and parenting skills, and cognitive training for working memory deficits. However, most of the available randomized controlled trials are short-term efficacy trials recruiting selected populations of patients and, as such, they are not fully informative for the daily clinical practice. Head-to-head trials, pragmatic trials, placebowithdrawal trials, network meta-analyses and individual patient data meta-analyses are encouraged in the field to bridge the gap between theoretical evidence and daily clinical practice

.....

Rev Neurol. 2017 Feb;64:S95-S100.

COMPARISON BETWEEN THE DIAGNOSIS OF ATTENTION DEFICIT HYPERACTIVITY DISORDER WITH THE DSM-5 AND NEUROPSYCHOLOGICAL EVALUATION OF THE EXECUTIVE FUNCTIONS.

Abad-Mas L, Caloca-Catala O, Mulas F, et al.

**INTRODUCTION**: The attention deficit-hyperactivity disorder (ADHD) has a prevalence among 3-7% in scholar population and it is associated with learning disabilities and executive dysfunctions. AIM: To study the relationship between the ADHD diagnostic through DSM-5 criteria and the neuropshychology evaluation of executive functions.

**SUBJECTS AND METHODS**: The sample of this study consisted in 50 subjects, 12 females and 38 males, with an age between 8 and 10 years old. To evaluate the inhibitory control, we used the Stroop Test and the Continuous Performance Test (CPT), to evaluate intelligence and working memory we use the Wechsler Intelligence Scale WISC-IV, to evaluate attention we used the CPT and Selective Attention Test.

**RESULTS**: There weren't significant differences between both subtypes of ADHD regarding working memory, on the other hand the female group had better abilities in cognitive flexibility task than males and subjects diagnosed with combined ADHD had more difficulties in inhibitory control.

**CONCLUSIONS**: We can confirm that the definition of ADHD in DSM-5 isn't enough as them are imprecise. Therefore, the disease definition it's performed by a specific evaluation of attention and inhibitory control mechanisms and its necessary a neuropshychological evaluation of these brain functions

.....

Rev Neurol. 2017 Feb;64:S105-S109.

CURRENT STATE OF THE ATTENTION DEFICIT HYPERACTIVITY DISORDER APPROACH IN NEUROPEDIATRICS.

Cardo E, Ros-Cervera G, Eiris-Punal J, et al.

**AIM**: To know the current state of the approach of attention deficit hyperactivity disorder (ADHD) in neuropediatricians.

**SUBJECTS AND METHODS**: A telematic survey was carried out to collect preliminary information on the interest, difficulties in the management and treatment of ADHD to the 437 fellowship of the Neuropediactric Spanish Society (SENEP).

RESULTS: Only 32.49% of the sent questionnaires were answered, with important geographic variability. 97.89% stated that 50% of their consultations were children with learning disabilities and ADHD. Regarding who started treatment for ADHD in their area, the majority answered that the neuropediatrician (57.97%), followed by the child psychiatrist (34.78%) and the primary care pediatrician (5.31%). The lack of a psychopedagogical study by the school (49.79%), followed by the lack of time in the consultation (29.11%), was cited as the greatest difficulty in the initial assessment of children with suspected ADHD. Concerning the difficulties in the follow-up, the biggest complaint was the lack of coordination between professionals, the school and parents. And, lastly, regarding the type of treatment use, most patients were on prolonged-release methylphenidate, a stable percentage using immediate release methylphenidate as a single or combined treatment, and in a lower range was the use of clonidine and atomoxetine, and an incipient use of lisdexamphetamine were observed. 80% of the patient showed adherence to pharmacological treatment after one year.

**CONCLUSIONS**: It is necessary to advance in the training and continuous education of our neuropediatric specialists in ADHD and to homogenize the clinical practice and coordination with education system in the Spanish territory

.....

Sch Psychol Q. 2018 Mar.

SLUGGISH COGNITIVE TEMPO AND STUDENT-TEACHER RELATIONSHIP QUALITY: SHORT-TERM LONGITUDINAL AND CONCURRENT ASSOCIATIONS.

## Holdaway AS, Becker SP.

Although sluggish cognitive tempo (SCT) is associated with poorer peer functioning, no study has examined SCT in relation to student–teacher relationship quality. The current study examined whether SCT, as rated by both teachers and children, was uniquely associated with poorer student–teacher relationship quality above and beyond child demographics and other mental health symptoms (i.e., attention-deficit/hyperactivity disorder [ADHD], oppositional defiant disorder/conduct disorder [ODD/CD], anxiety/depression). Gender was examined as a possible moderator of the association between SCT and student–teacher relationship quality. Participants were 176 children in 1st–6th grades and their teachers. Teachers rated children's SCT and other mental health symptoms in the fall semester (T1) and the student–teacher relationship (conflict and closeness) 6 months later (T2). Children provided self-ratings of SCT at T2. Above and beyond age, gender, and other mental health symptoms, teacher-rated SCT at T1 was associated with greater student–teacher conflict at T2. This association was qualified by a SCT x Gender interaction, with SCT associated with greater conflict, above and beyond covariates. In addition, teacher-rated SCT at T1 was the only mental health dimension to be significantly associated with less student–teacher closeness at T2. Findings extend the social difficulties

associated with SCT to the student-teacher relationship, an important relationship associated with children's academic and socioemotional outcomes

.....

Soc Psychiatry Psychiatr Epidemiol. 2017 Aug;52:963-77.

DISPENSING OF PSYCHOTROPIC MEDICATION AMONG 400,000 IMMIGRANTS IN THE NETHERLANDS.

Termorshuizen F, Selten JP, Heerdink ER.

**PURPOSE**: Previously, a high prevalence of certain psychiatric disorders was shown among non-Western immigrants. This study explores whether this results in more prescriptions for psychotropic medication.

**METHODS**: Data on dispensing of medication among adults living in the four largest Dutch cities in 2013 were linked to demographic data from Statistics Netherlands. Incident (i.e., following no dispensing in 2010-2012) and prevalent dispensing among immigrants was compared to that among native Dutch (N = 1,043,732) and analyzed using multivariable Poisson and logistic regression.

**RESULTS**: High adjusted Odds Ratios (ORadj) of prevalent and high Incidence Rate Ratios (IRRadj) of incident dispensing of antipsychotics were found among Moroccan (N = 115,455) and Turkish individuals (N = 105,460), especially among young Moroccan males (ORadj = 3.22 [2.99-3.47]). Among Surinamese (N = 147,123) and Antillean individuals (N = 41,430), slightly higher rates of dispensed antipsychotics were found and the estimates decreased after adjustment. The estimates for antipsychotic dispensing among the Moroccan and Turkish increased, following adjustment for household composition. Rates for antidepressant dispensing among Turkish and Moroccan subjects were high (Moroccans: ORadj = 1.74 [1.70-1.78]). Among Surinamese and Antillean subjects, the rates for antidepressant dispensing were low and the ORadj lagged behind the IRRadj (Surinamese: 0.69 [0.67-0.71] vs. 1.06 [1.00-1.13]). Similar results were found for anxiolytics. For ADHD medication, lower dispensing rates were found among all migrant groups.

**CONCLUSIONS**: The findings agree with earlier reports of more mental health problems among Moroccan and Turkish individuals. Surinamese/Antillean individuals did not use psychotropic drugs at excess and discontinued antidepressants and anxiolytics earlier. The data strongly suggest under-treatment for ADHD in all ethnic minority groups

.....

Toxicology and Applied Pharmacology, 2018.

EARLY LIFE EXPOSURE TO AIR POLLUTION PARTICULATE MATTER (PM) AS RISK FACTOR FOR ATTENTION DEFICIT/HYPERACTIVITY DISORDER (ADHD): NEED FOR NOVEL STRATEGIES FOR MECHANISMS AND CAUSALITIES.

Myhre O, et al.

Epidemiological studies have demonstrated that air pollution particulate matter (PM) and adsorbed toxicants (organic compounds and trace metals) may affect child development already in utero. Recent studies have also indicated that PM may be a risk factor for neurodevelopmental disorders (NDDs). A pattern of increasing prevalence of attention deficit/hyperactivity disorder (ADHD) has been suggested to partly be linked to environmental pollutants exposure, including PM. Epidemiological studies suggest associations between pre- or postnatal exposure to air pollution components and ADHD symptoms. However, many studies are cross-sectional without possibility to reveal causality. Cohort studies are often small with poor exposure characterization, and confounded by traffic noise and socioeconomic factors, possibly overestimating the study associations. Furthermore, the mechanistic knowledge how exposure to PM during early brain development may contribute to increased risk of ADHD symptoms or cognitive deficits is limited. The closure of this knowledge gap requires the combined use of well-designed longitudinal cohort studies, supported by mechanistic in vitro studies. As ADHD has profound consequences for the children affected and their families, the identification of preventable risk factors such as air pollution exposure should be of high priority

Trials. 2018;19.

BRIGHT LIGHT THERAPY VERSUS PHYSICAL EXERCISE TO PREVENT CO-MORBID DEPRESSION AND OBESITY IN ADOLESCENTS AND YOUNG ADULTS WITH ATTENTION-DEFICIT / HYPERACTIVITY DISORDER: STUDY PROTOCOL FOR A RANDOMIZED CONTROLLED TRIAL.

Mayer JS, Hees K, Medda J, et al.

Background: The risk for major depression and obesity is increased in adolescents and adults with attention-deficit / hyperactivity disorder (ADHD) and adolescent ADHD predicts adult depression and obesity. Non-pharmacological interventions to treat and prevent these co-morbidities are urgently needed. Bright light therapy (BLT) improves day-night rhythm and is an emerging therapy for major depression. Exercise intervention (EI) reduces obesity and improves depressive symptoms. To date, no randomized controlled trial (RCT) has been performed to establish feasibility and efficacy of these interventions targeting the prevention of co-morbid depression and obesity in ADHD. We hypothesize that the two manualized interventions in combination with mobile health-based monitoring and reinforcement will result in less depressive symptoms and obesity compared to treatment as usual in adolescents and young adults with ADHD.

**Methods**: This trial is a prospective, pilot phase-IIa, parallel-group RCT with three arms (two add-on treatment groups [BLT, EI] and one treatment as usual [TAU] control group). The primary outcome variable is change in the Inventory of Depressive Symptomatology total score (observer-blinded assessment) between baseline and ten weeks of intervention. This variable is analyzed with a mixed model for repeated measures approach investigating the treatment effect with respect to all three groups. A total of 330 participants with ADHD, aged 14 - < 30 years, will be screened at the four study centers. To establish effect sizes, the sample size was planned at the liberal significance level of +| = 0.10 (two-sided) and the power of 1-+| = 80% in order to find medium effects. Secondary outcomes measures including change in obesity, ADHD symptoms, general psychopathology, health-related quality of life, neurocognitive function, chronotype, and physical fitness are explored after the end of the intervention and at the 12-week follow-up. **Discussion**: This is the first pilot RCT on the use of BLT and EI in combination with mobile health-based monitoring and reinforcement targeting the prevention of co-morbid depression and obesity in adolescents and young adults with ADHD. If at least medium effects can be established with regard to the prevention of depressive symptoms and obesity, a larger scale confirmatory phase-III trial may be warranted

.....

Ups J Med Sci. 2017 Jun;122:119-26.

GAMBLING FREQUENCY AND SYMPTOMS OF ATTENTION-DEFICIT HYPERACTIVITY DISORDER IN RELATION TO PROBLEM GAMBLING AMONG SWEDISH ADOLESCENTS: A POPULATION-BASED STUDY.

Hellstrom C, Wagner P, Nilsson KW, et al.

**AIM**: To investigate the associations between gambling frequency, attention-deficit hyperactivity disorder (ADHD) symptoms, and problem gambling among adolescent boys and girls. One hypothesis was that adolescents with increased ADHD symptoms have a higher frequency of gambling compared to adolescents with fewer ADHD symptoms.

**METHOD**: A population-based sample of adolescents (aged 15-18 years) completed a questionnaire on demographics, gambling habits, ADHD symptoms, and problematic gambling; 1412 adolescents (from 4440 sampled) with gambling experience were included in the final sample.

**RESULTS**: A zero-inflated negative binomial regression analysis revealed that increased ADHD symptoms, higher gambling frequency, and higher age were associated with lower odds for being non-susceptible to gambling problems. Moreover, gambling frequency interacted with ADHD symptoms in predicting probability of being non-susceptible to gambling problems. However, when analysing those already susceptible to problem gambling, ADHD symptoms did not modify the effect of gambling frequency on the expected magnitude of gambling problems. In susceptible individuals, problem gambling increased with both increased ADHD symptoms and increased gambling frequency, but the level of problems due to gambling frequency did not change depending on the ADHD symptom level. There was an interaction effect between sex and gambling frequency in relation to gambling problems.

**CONCLUSIONS**: Adolescents with ADHD symptoms seem to be more sensitive to gambling, in terms of being susceptible to developing gambling problems. However, once susceptible, adolescents with ADHD symptoms are affected by gambling frequency similarly to other susceptible participants

.....

World J Biol Psychiatry. 2018;1-12.

DECREASED RESTING GAMMA ACTIVITY IN ADULT ATTENTION DEFICIT/HYPERACTIVITY DISORDER.

Tombor L, Kakuszi B, Papp S, et al.

**OBJECTIVES**: To delineate task-free gamma activity in adult ADHD and healthy control subjects based on high-density EEG recordings. Relationship of gamma activity with symptom severity was also examined, since gamma activity is considered to be an index of network functions in the brain that underlie higher-order cognitive processes.

**METHODS**: Spontaneous EEG was recorded in adult ADHD subjects (N = 42; 25 methylphenidate-naïve and 17 on methylphenidate treatment) and controls (N = 59) with eyes open. EEG absolute power gamma was investigated in the gamma1 (30.25-39 Hz) and gamma2 (39.25-48 Hz) frequency bands.

**RESULTS**: Gamma1 and gamma2 activity was diminished in ADHD compared with healthy control subjects. The difference between ADHD and controls was the most pronounced in the right centroparietal region for both gamma1 and gamma2. Inverse associations were found between gamma1 and gamma2 activity and ADHD symptoms in centroparietal scalp regions.

**CONCLUSIONS**: Gamma activity is reduced in adult ADHD, and the reduction has a predominantly right centroparietal distribution. Our findings are consistent with childhood ADHD literature with respect to diminished posterior gamma activity in patients, which may reflect altered dorsal attention network functions. Gamma abnormalities might provide a link between neurophysiological functioning and neuropsychological deficiencies, thereby offering an opportunity to investigate the neurobiological mechanisms that underlie the clinical symptoms of ADHD

.....

World J Biol Psychiatry. 2018;1-9.

ATTENTION-DEFICIT/HYPERACTIVITY DISORDER IS ASSOCIATED WITH REDUCED LEVELS OF SERUM LOW-DENSITY LIPOPROTEIN CHOLESTEROL IN ADOLESCENTS. DATA FROM THE POPULATION-BASED GERMAN KIGGS STUDY.

Pinho R, Wang B, Becker A, et al.

**OBJECTIVES**: Attention-deficit/hyperactivity disorder (ADHD) is a multifactorial, complex and the most common neurodevelopmental disorder in childhood. In this analysis, we tested the hypothesis that altered serum lipid patterns are associated with ADHD.

**METHODS**: Using data from the nationwide, population-based German Health Interview and Examination Survey for Children and Adolescents (KiGGS), we compared serum levels of total cholesterol, high-density (HDL) and low-density lipoprotein (LDL) cholesterol, and also triglycerides, in participants with physician-diagnosed and/or suspected ADHD, as defined by a value of ≥7 on the hyperactivity-inattention subscale of the Strengths and Difficulties Questionnaire (SDQ), with non-ADHD controls.

**RESULTS**: Among 6,898 participants aged between 11 and 17 years, 666 (9.7%) had a physician-based diagnosis of ADHD and/or suspected ADHD. We found correlations between the parent-rated SDQ scores on the hyperactivity-inattention subscale and concentrations of triglycerides (r = 0.064, p < .001), total cholesterol (r = -0.026, p = .033), HDL cholesterol (r = -0.059, p < .001) and LDL cholesterol (r = -0.027, p = .031). In multivariate models, low serum levels of LDL cholesterol remained a significant predictor of ADHD (Exp( $\beta$ ) = 0.382, 95% confidence interval = 0.165-0.888, p = .025).

**CONCLUSIONS**: Our findings in a large, nationwide and representative sample of German adolescents demonstrated a small, but significant and inverse link between LDL cholesterol levels and symptoms of ADHD. Further studies are required to decipher the biochemical mechanisms behind this relationship

Zhonghua Yi Xue Yi Chuan Xue Za Zhi. 2017 Dec;34:844-48.

EXPLORATION OF COMMON BIOLOGICAL PATHWAYS FOR ATTENTION DEFICIT HYPERACTIVITY DISORDER AND LOW BIRTH WEIGHT.

Xiang B, Yu M, Liang X, et al.

**OBJECTIVE**: To explore common biological pathways for attention deficit hyperactivity disorder (ADHD) and low birth weight (LBW).

**METHODS**: Thei-Gsea4GwasV2 software was used to analyze the result of genome-wide association analysis (GWAS) for LBW (pathways were derived from Reactome), and nominally significant (P< 0.05, FDR< 0.25) pathways were tested for replication in ADHD. Significant pathways were analyzed with DAPPLE and Reatome FI software to identify genes involved in such pathways, with each cluster enriched with the gene ontology (GO). The Centiscape2.0 software was used to calculate the degree of genetic networks and the betweenness value to explore the core node (gene). Weighed gene co-expression network analysis (WGCNA) was then used to explore the co-expression of genes in these pathways. With gene expression data derived from BrainSpan, GO enrichment was carried out for each gene module.

**RESULTS**: Eleven significant biological pathways was identified in association with LBW, among which two (Selenoamino acid metabolism and Diseases associated with glycosaminoglycan metabolism) were replicated during subsequent ADHD analysis. Network analysis of 130 genes in these pathways revealed that some of the sub-networksare related with morphology of cerebellum, development of hippocampus, and plasticity of synaptic structure. Upon co-expression network analysis, 120 genes passed the quality control and were found to express in 3 gene modules. These modules are mainly related to the regulation of synaptic structure and activity regulation.

**CONCLUSION**: ADHD and LBW share some biological regulation processes. Anomalies of such proces sesmay predispose to ADHD

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

# IRCCS ISTITUTO DI RICERCHE FARMACOLOGICHE MARIO NEGRI DIPARTIMENTO DI SALUTE PUBBLICA Laboratorio per la Salute Materno Infantile

Via Giuseppe La Masa, 19 - 20156 Milano MI - Italia - www.marionegri.it tel +39 02 39014.511 - fax +39 02 3550924 - mother\_child@marionegri.i