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2. Segnalazioni

   **Prof. Francesco Barale**
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   **Prof. Cristiano Termine**
   Seminario “I DISTURBI DELL’APPRENDIMENTO IN UNA SOCIETÀ DISATTENTA”
   16 aprile 2014, Milano
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**MUCOPOLYSACCHARIDOSIS TYPE III (SANFILIPPO SYNDROME) AND MISDIAGNOSIS OF IDIOPATHIC DEVELOPMENTAL DELAY, ATTENTION DEFICIT/HYPERACTIVITY DISORDER OR AUTISM SPECTRUM DISORDER.**

**Wijburg FA, Wegrzyn G, Burton BK, et al.**

Mucopolysaccharidosis III is a rare genetic disease characterized by progressive cognitive decline and severe hyperactivity that does not respond to stimulants. Somatic features are relatively mild. Patients are often initially misdiagnosed as having idiopathic developmental delay, attention deficit/hyperactivity disorder and/or autism spectrum disorders, putting them at risk for unnecessary testing and treatments.

**CONCLUSION:** Children with developmental or speech delay, especially those with a characteristic somatic feature or behavioural abnormalities, should be screened for MPS III.

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Per la ricerca degli articoli pubblicati nella letteratura scientifica nel mese in esame sono state consultate le banche dati Medline, Embase, PsycINFO e PsycArticle utilizzando le seguenti parole chiave (o i loro sinonimi): 'Attention deficit disorder', 'Attention deficit hyperactivity disorder', 'Infant', 'Child', 'Adolescent', 'Human'. Sono qui riportate le referenze considerate rilevanti e pertinenti.
NEUROBEHAVIOURAL DEVELOPMENT OF PRESCHOOL-AGE CHILDREN BORN TO ADDICTED MOTHERS GIVEN OPIATE MAINTENANCE TREATMENT WITH BUPRENORPHINE DURING PREGNANCY.
Sundelin W, V, Sarman I.
AIM: To study the neurobehavioural development and somatic growth of children at preschool-age born to opioid-addicted mothers given opiate maintenance treatment (OMT) with buprenorphine during pregnancy.
METHODS: Twenty-eight children, whose 21 opiate-addicted mothers were treated with OMT during pregnancy and accepted participation to the study, went through a battery of neurobehavioural tests (WPPSI-R, McCarthy, BROWN and SDQ). Twenty-five children fulfilled the tests at an age of 5-6 years.
RESULTS: The children showed evidence of serious visual motor and attention problems in the field of performance (WPPSI-R scales) and major problems in the field of motor skills and memory abilities (McCarthy Scales). The results of behavioural tests also showed significantly elevated levels of hyperactivity, impulsivity and attention problems on the attention deficit hyperactivity disorder (ADHD) scale in BROWN and in SDQ tests estimated by the teachers, while the parents estimated no problems for their children. Regarding the outcomes, there were no significant differences in terms of neonatal abstinence syndrome, gender or socio-economic factors. The somatic growth of the children corresponded to the mean values of the normal population in weight, length and head circumference at birth and at preschool-age, respectively.
CONCLUSION: Children to opiate-addicted mothers with buprenorphine maintenance treatment during pregnancy constitute a risk population, which should be recognized before start of the school. Whether the effects are associated with buprenorphine exposition during foetal life or not are discussed and need further investigation.

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Actas Esp Psiquiatr. 2013 Jan;41:44-51.
IS PSYCHOLOGICAL TREATMENT EFFICACIOUS FOR ATTENTION DEFICIT HYPERACTIVITY DISORDER (ADHD)? REVIEW OF NON-PHARMACOLOGICAL TREATMENTS IN CHILDREN AND ADOLESCENTS WITH ADHD.
Serrano-Troncoso E, Guidi M, Alda-Diez JA.
INTRODUCTION: Attention deficit hyperactivity disorder (ADHD) is the most prevalent psychiatric disorder in children and adolescents, and has a great impact on the psychological development of affected patients. Even though its efficacy is proven, the use of medication for ADHD has several limitations, and non-pharmacological interventions are considered a necessary component of treatment.
METHODOLOGY: This work is a review of evidence-based non-pharmacological treatments with demonstrated efficacy for ADHD in children and adolescents, analyzed by age groups.
RESULTS: Non-pharmacological treatments that have shown scientific evidence of efficacy are psychological and psychoeducational interventions. Psychological interventions include behavioral therapy, parent training (PT) and social skills training. Psychoeducational interventions include a set of practices to improve learning and are carried out in the school setting. Scientific evidence of efficacy in preschool children is limited to PT, while different psychological and psychoeducational interventions have been shown to be beneficial in school-age children. The available evidence for non-pharmacological treatment in adolescence is so far insufficient.
CONCLUSIONS: Though more randomized controlled trials are necessary for non-pharmacological interventions to become established practices, there are clear indications of their efficacy. For more severe cases of ADHD, a combination of non-pharmacological and pharmacological treatment is recommended.

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PEDIATRIC PSYCHOPHARMACOLOGY IN PRIMARY CARE: A CONCEPTUAL FRAMEWORK.
Riddle MA, DosReis S, Reeves GM, et al.
In a 2009 policy statement focused on children's mental health, the American Academy of Pediatrics recommended that pediatric primary care physicians achieve competence in initiating care for children with
attention-deficit/hyperactivity disorder (ADHD), anxiety, depression, and substance use/abuse. Because treatment for 3 of these conditions—ADHD, anxiety, and depression—may, under certain conditions, include medication, the primary purpose of this article is to offer guidance to assist primary care physicians in decision-making about their use of psychotropic medications for these conditions. A few medications with proven efficacy and safety are emphasized. Secondarily, other medications that may be useful for other disorders are noted.


PHARMACOTHERAPY OF INATTENTION AND ADHD IN ADOLESCENTS.

This article reviews the current use of stimulants in adolescents. The evidence base for treatment of attention-deficit/hyperactivity disorder (ADHD) in adolescents is meager compared with that of ADHD in children, and much recent research of older populations with ADHD has been directed toward adults rather than adolescents. The structure of psychosocial treatment of ADHD differs across developmental ranges. For example, in children, treatment of ADHD uses direct behavior modification via parents and teachers. Treatment approaches then change toward contracting in adolescents (acknowledging the emerging independence common at this age) and toward self-management and coaching in adults. Medication for ADHD, however, does not substantially differ across developmental epochs. In supplementation of data, specifically on adolescence, much of our understanding of treating adolescents comes from upward or downward extension of the child and adult data. Symptomatic treatment (treatment for inattention, hyperactivity, or impulsive behavior) has always been a parallel approach to diagnostic and developmentally specific selection of treatment based on an incomplete literature. In recognition, this article assumes that inference from children or adults to adolescents, in the absence of adolescent-specific data, is commonplace and often confirmed with clinical experience. Such inferences, in the face of literature gaps, in no way obviate the need for continued research focused on adolescence.


FURTHER DEVELOPMENT OF A NEUROBEHAVIORAL PROFILE OF FETAL ALCOHOL SPECTRUM DISORDERS.
Mattson SN, Roesch SC, Glass L, et al.

BACKGROUND: Heavy prenatal alcohol exposure (AE) results in a broad array of neurobehavioral deficits. Recent research has focused on identification of a neurobehavioral profile or profiles that will improve the identification of children affected by AE. This study aimed to build on our preliminary neurobehavioral profile to improve classification accuracy and test the specificity of the resulting profile in an alternate clinical group.

METHODS: A standardized neuropsychological test battery was administered to 3 groups of children: subjects with AE (n=209), typically developing controls (CON, n=185), and subjects with attention-deficit/hyperactivity disorder (ADHD, n=74). We assessed a large sample from 6 sites in the United States and South Africa, using standardized methodology. Data were analyzed using 3 latent profile analyses including (i) subjects with fetal alcohol syndrome (FAS) and controls, (ii) subjects with AE without FAS and controls, and (iii) subjects with AE (with or without FAS) and subjects with ADHD.

RESULTS: Classification accuracy was moderate but significant across the 3 analyses. In analysis 1, overall classification accuracy was 76.1% (77.2% FAS, 75.7% CON). In the second analysis, overall classification accuracy was 71.5% (70.1% AE/non-FAS, 72.4% CON). In the third analysis, overall classification accuracy was 73.9% (59.8% AE, 75.7% ADHD). Subjects that were misclassified were examined for systematic differences from those that were correctly classified.

CONCLUSIONS: The results of this study indicate that the neuropsychological effects of AE are clinically meaningful and can be used to accurately distinguish alcohol-affected children from both typically developing children and children with ADHD. Further, in combination with other recent studies, these data suggest that approximately 70% of children with heavy prenatal alcohol exposure are neurobehaviorally affected, while the remaining 30% are spared these often-devastating consequences, at least those in the
domains under study. Refining the neurobehavioral profile will allow improved identification and treatment development for children affected by prenatal alcohol exposure.


ASSOCIATION OF DOPAMINE TRANSPORTER GENE VARIANTS WITH CHILDHOOD ADHD FEATURES IN BIPOLAR DISORDER.


Bipolar disorder (BD) and attention deficit hyperactivity disorder (ADHD) exhibit remarkably high rates of comorbidity, as well as patterns of familial co-segregation. Epidemiological data suggests that these disorders either share a common genetic architecture or that ADHD features in BD may represent an etiologically distinct subtype. We previously used the Wender Utah Rating Scale (WURS) to assess ADHD features in BD families and identified three heritable factors relating to impulsivity, mood instability, and inattention. Linkage analysis revealed a LOD score of 1.33 for the inattention factor on 5p15.3 near the dopamine transporter gene (DAT1), which has been associated with both BD and ADHD. Pharmacological evidence also suggests a role for DAT in both disorders. We have now evaluated the association of ten DAT1 variants for the WURS total score and factors in an overlapping sample of 87 BD families. Significant associations for three SNPs were observed across the WURS measures, notably for a SNP in intron 8 with the WURS total score (P=0.007) and for variants in introns 9 and 13 with mood instability (P=0.009 and 0.004, respectively). Analysis of an independent sample of 52 BD cases and 46 healthy controls further supported association of the intron 8 variant with mood instability (P=0.005), and a combined analysis confirmed the associations of this SNP with WURS total score. Impulsivity and mood instability (P=0.002, 0.007, and 8 x 10(-4), respectively). These data suggest that variants within DAT1 may predispose to a subtype of BD characterized by early prodromal features that include attentional deficits.


DO WE HAVE TO WAIT FOR A CHILD TO SUFFER A SERIOUS INJURY TO SUSPECT A HYPERACTIVITY/ATTENTION DEFICIT DISORDER? A CASE-CONTROL STUDY OF PATIENTS ADMITTED TO PICU.

Crujeiras M, V, Gonzalez PY, Perez GL, et al.

Arch Dis Child. 2013.

RISK OF SUBSEQUENT ATTENTION DEFICIT-HYPERACTIVITY DISORDER IN CHILDREN WITH FEBRILE SEIZURES.

Ku YC, Muo CH, Ku CS, et al.

Objective: In this study, we obtained relevant data from a nationwide cohort database to investigate the risk of attention deficit-hyperactivity disorder (ADHD) in children with a history of febrile seizures (FS).

Methods: We identified 1081 children with FS as the case cohort, and the date of diagnosis was used as an index date. Four controls were matched randomly with each case based on age, sex, urbanisation level, parents’ occupation, and index date. We applied Cox's proportional hazards regression to estimate the HR and CI of FS-associated ADHD.

Results: After 11 years of follow-up, the incidence of ADHD for the FS and control cohorts is 7.83 and 4.72 per 1000 person-years, respectively. The FS cohort was 1.66 times more at risk of ADHD occurrence (95% CI 1.27 to 2.18) than the control cohort. The risk of developing ADHD increased in conjunction with the frequency of FS-related visits.

Conclusions: FS may increase the risk of subsequent ADHD occurrence in children. Children who visited physicians for FS more than twice had a significantly higher cumulative incidence of ADHD.

ADHD IN IDIOPATHIC EPILEPSY.
*Duran MHC, Guimaraes CA, Montenegro MA, et al.*

Our aim was to clarify the correlation of attention deficit hyperactivity disorder (ADHD) with epilepsy and behavior problems. This was a cross-sectional study. Sixty children with idiopathic epilepsy were interviewed using the MTA-SNAP IV Teacher and Parent Rating Scale, Vineland Adaptive Behavior Scales and Conners' Rating Scales. We used the chi-square test to analyze the correlation of epilepsy variables in patients with and without ADHD with a significance level of 0.05. Eight patients had ADHD symptoms (13%), seven had the inattentive ADHD subtype and only three had behavioral problems. When epileptic patients with and without ADHD symptoms were compared we found no significant difference in regard to epilepsy variables. All patients were controlled and 43% were either without AED or undergoing withdrawal. Our study revealed a low comorbidity of ADHD symptoms and epilepsy due to low interference of seizures and drug treatment on the comorbid condition.

UNDERSTANDING THE SENSORY EXPERIENCES OF YOUNG PEOPLE WITH AUTISM SPECTRUM DISORDER: A PRELIMINARY INVESTIGATION.
*Ashburner J, Bennett L, Rodger S, et al.*

**BACKGROUND/AIM:** Unusual responses to sensations can impact upon the daily activities for individuals with autism spectrum disorder. Current understandings of these sensory experiences have been drawn from the proxy reports from parents/caregivers, standardised self-report questionnaires and autobiographical accounts. As sensory experiences are intensely personal, the first-hand accounts of people with autism spectrum disorder may have greater validity than caregiver reports, but these have never been systematically researched. This study explored the utility of using a semi-structured interview protocol augmented with visual cues to facilitate our understanding of the way people with autism spectrum disorder experience sensory input, and use coping strategies to manage sensory issues that interfere with participation.

**METHOD:** A semi-structured interview augmented by visual cues was used to investigate the sensory experiences of three adolescent males with autism spectrum disorder. As is common in this population, two of the participants also had a diagnosis of Attention Deficit Hyperactivity Disorder and were taking stimulant medication.

**RESULTS:** Participants shared a preference for expected, predictable and controllable sensory input, whereas unexpected, unpredictable and uncontrollable sensations were perceived as unpleasant. A heightened awareness of and difficulty filtering extraneous sensory input, high levels of movement seeking and an over-focus on salient sensory input were also described. Strategies employed to manage sensory challenges included avoiding, increasing predictability and control and meta-cognitive adaptations.

**CONCLUSIONS:** Further research involving a larger sample of participants is recommended to determine the utility of using a semi-structured interview protocol augmented with visual cues to understand the sensory experiences of individuals with high-functioning autism spectrum disorder.

THE DSM-5 CHANGES AND ADHD: MORE THAN A TWEAK OF TERMS.
*Prosser B, Reid R.*

In this opinion, author states that psychiatric diagnosis is based on symptom clusters that describe clinical syndromes rather than specific disorders with clear underlying pathophysiologic abnormalities. Individual diagnostic categories are heterogeneous and of uncertain aetiology, despite decades of research. There is some evidence to support this proposition. The associations of NMDAR and VGKC complex antibodies with clinical presentations are strong, biologically plausible and consistent across studies. Patients with higher antibody titres develop more severe illness and have poorer outcomes. MRI abnormalities correlate with severity of clinical disease and antibody titres. Clinical improvement correlates temporally and
quantitatively with a fall in antibody titres, resolution of MRI abnormalities and tumour removal. Finally, author suggests that treatment should be in collaboration with neurology and other general hospital colleagues.


**BAIAP2 EXHIBITS ASSOCIATION TO CHILDHOOD ADHD ESPECIALLY PREDOMINANTLY INATTENTIVE SUBTYPE IN CHINESE HAN SUBJECTS.**

**Liu L, Sun L, Li ZH, et al.**

**Background:** Attention-deficit/hyperactivity disorder (ADHD) is a common chronic neurodevelopmental disorder with a high heritability. Much evidence of hemisphere asymmetry has been found for ADHD probands from behavioral level, electrophysiological level and brain morphology. One previous research has reported possible association between BAIAP2, which is asymmetrically expressed in the two cerebral hemispheres, with ADHD in European population. The present study aimed to investigate the association between BAIAP2 and ADHD in Chinese Han subjects.

**Methods:** A total of 1,397 ADHD trios comprised of one ADHD proband and their parents were included for family-based association tests. Independent 569 ADHD cases and 957 normal controls were included for case-control studies. Diagnosis was performed according to the DSM-IV criteria. Nine single nucleotide polymorphisms (SNPs) of BAIAP2 were chosen and performed genotyping for both family-based and case-control association studies.

**Results:** Transmission disequilibrium tests (TDTs) for family-based association studies showed significant association between the CA haplotype comprised by rs3934492 and rs9901648 with predominantly inattentive type (ADHD-I). For case-control study, chi-square tests provided evidence for the contribution of SNP rs4969239, rs3934492 and rs4969385 to ADHD and its two clinical subtypes, ADHD-I and ADHD-C. However, only the associations for ADHD and ADHD-I retained significant after corrections for multiplicity or logistic regression analyses adjusting the potential confounding effect of gender and age.

**Conclusions:** These above results indicated the possible involvement of BAIAP2 in the etiology of ADHD, especially ADHD-I.

Behav Brain Res. 2014 Feb;259:97-105.

**DEFICITS IN RESPONSE INHIBITION CORRELATE WITH OCULOMOTOR CONTROL IN CHILDREN WITH FETAL ALCOHOL SPECTRUM DISORDER AND PRENATAL ALCOHOL EXPOSURE.**

**Paolozza A, Rasmussen C, Pei J, et al.**

Children with fetal alcohol spectrum disorder (FASD) or prenatal alcohol exposure (PAE) frequently exhibit impairment on tasks measuring inhibition. The objective of this study was to determine if a performance-based relationship exists between psychometric tests and eye movement tasks in children with FASD. Participants for this dataset were aged 5–17 years and included those diagnosed with an FASD (n =72), those with PAE but no clinical FASD diagnosis (n =21), and typically developing controls (n =139). Participants completed a neurobehavioral test battery, which included the NEPSY-II subtests of auditory attention, response set, and inhibition. Each participant completed a series of saccadic eye movement tasks, which included the antisaccade and memory-guided tasks. Both the FASD and the PAE groups performed worse than controls on the subtest measures of attention and inhibition. Compared with controls, the FASD group made more errors on the antisaccade and memory-guided tasks. Among the combined FASD/PAE group, inhibition and switching errors were negatively correlated with direction errors on the antisaccade task but not on the memory-guided task. There were no significant correlations in the control group. These data suggests that response inhibition deficits in children with FASD/PAE are associated with difficulty controlling saccadic eye movements which may point to overlapping brain regions damaged by prenatal alcohol exposure. The results of this study demonstrate that eye movement control tasks directly relate to outcome measures obtained with psychometric tests that are used during FASD diagnosis, and
may therefore help with early identification of children who would benefit from a multidisciplinary diagnostic assessment.

**ELECTROENCEPHALOGRAM SYNCHRONIZATION ANALYSIS FOR ATTENTION DEFICIT HYPERACTIVITY DISORDER CHILDREN.**
This study investigated the changes in synchronization of different electroencephalogram (EEG) bands in attention deficit hyperactivity disorder (ADHD) children. EEG data were obtained from 13 children diagnosed with ADHD and 13 normal control children in the resting state. The statistical dependencies between each EEG channel were generated by calculating synchronization likelihood. The differences of synchronization between the ADHD and control groups were statistically evaluated. Overall, the synchronization was significantly higher in the ADHD group in the alpha and beta bands. The present study found that synchronization was significantly altered in the fast EEG bands in patients with ADHD. These findings may enhance our understanding for the relationship between ADHD and cerebral dysfunction.

**RESPONSE TIME OF VISUAL MATCHING TASK AND HEART RATE IN CHILDREN WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER (ADHD).**
Kim HJ, Kim HS, Choi MH, et al.
The purpose of this study was to investigate the relation between response time of visual matching task and heart rate (HR) in children with Attention Deficit Hyperactivity Disorder (ADHD). Thirty boys who were diagnosed with ADHD and are under treatment participated in the study. The experiment consisted of three phases, a total of 5 min with rest phase, control phase, and visual matching task phase. HR was measured during each phase. The HR in visual matching task phase increased, compared to that in rest phase. There was a negative correlation between response time of visual matching task and magnitude of the HR in the visual matching task phase. In other words, as HR increased, response time of the visual matching task decreased. This means that increasing in HR increased the supply of oxygen by fast circulation of blood for cognitive processing and this induced the improvement of cognitive ability in the ADHD children. This means that increasing HR increased the supply of oxygen by fast circulation of blood for cognitive processing and this induced the improvement of cognitive ability in the ADHD children. The result of this study supports previous studies that the administration of high oxygen concentration can positively affect the cognitive performance of the ADHD children. The results of the present and previous studies also may provide scientific evidence that can be used for treating patients with cognitive problems such as ADHD.

**FUNCTIONAL GENOMICS OF ATTENTION-DEFICIT/HYPERACTIVITY DISORDER (ADHD) RISK ALLELES ON DOPAMINE TRANSPORTER BINDING IN ADHD AND HEALTHY CONTROL SUBJECTS.**
**BACKGROUND:** The main aim of this study was to examine the relationship between dopamine transporter (DAT) binding in the striatum in individuals with and without attention-deficit/hyperactivity disorder (ADHD), attending to the 3'-untranslated region of the gene (3'-UTR) and intron8 variable number of tandem repeats (VNTR) polymorphisms of the DAT (SLC6A3) gene.

**METHODS:** Subjects consisted of 68 psychotropic (including stimulant)-naive and smoking-naive volunteers between 18 and 55 years of age (ADHD n=34; control subjects n=34). Striatal DAT binding was measured with positron emission tomography with 11C altropane. Genotyping of the two DAT (SLC6A3) 3'-UTR and intron8 VNTRs used standard protocols.
RESULTS: The gene frequencies of each of the gene polymorphisms assessed did not differ between the ADHD and control groups. The ADHD status (t=2.99; p<.004) and 3'-UTR of SLC6A3 9 repeat carrier status (t = 2.74; p<.008) were independently and additively associated with increased DAT binding in the caudate. The ADHD status was associated with increased striatal (caudate) DAT binding regardless of 3'-UTR genotype, and 3'-UTR genotype was associated with increased striatal (caudate) DAT binding regardless of ADHD status. In contrast, there were no significant associations between polymorphisms of DAT intron8 or the 3'-UTR-intron8 haplotype with DAT binding.

CONCLUSIONS: The 3'-UTR but not intron8 VNTR genotypes were associated with increased DAT binding in both ADHD patients and healthy control subjects. Both ADHD status and the 3'-UTR polymorphism status had an additive effect on DAT binding. Our findings suggest that an ADHD risk polymorphism (3'-UTR) of SLC6A3 has functional consequences on central nervous system DAT binding in humans.

GENETIC OVERLAP BETWEEN EVOKED FRONTOCENTRAL THETA-BAND PHASE VARIABILITY, REACTION TIME VARIABILITY, AND ATTENTION-DEFICIT/HYPERACTIVITY DISORDER SYMPTOMS IN A TWIN STUDY.

Background: Electrophysiological and hemodynamic activity is altered in attention-deficit/hyperactivity disorder (ADHD) during tasks requiring cognitive control. Frontal midline theta oscillations are a cortical correlate of cognitive control influencing behavioral outcomes including reaction times. Reaction time variability (RTV) is consistently increased in ADHD and is known to share genetic effects with the disorder. The etiological relationship between the cognitive control system, RTV, and ADHD is unknown. In a sample of twins selected for ADHD and matched control subjects, we aimed to quantify the strength of the phenotypic, genetic, and environmental relationships between event-related midline theta oscillations, RTV, and ADHD.

Methods: Our sample included 134 participants aged 12 to 15 years: 67 twin pairs (34 monozygotic; 33 dizygotic) with concordance or discordance for ADHD symptomatology assessed at 8, 10, and 12 years of age. Our main outcome measures were frontal midline theta activity, derived from both channel and source decomposed electroencephalographic data, and behavioral performance on a response-choice arrow flanker task known to elicit theta activity.

Results: Variability in stimulus event-related theta phase from frontal midline cortex is strongly related to both RTV and ADHD, both phenotypically and genetically.

Conclusions: This is the first finding to confirm the genetic link between the frontal midline cognitive control system and ADHD and the first to identify a genetically related neurophysiological marker of RTV in ADHD. Variability in the timing of the theta signal in ADHD may be part of a dysfunctional brain network that impairs regulation of task-relevant responses in the disorder.

REDUCED CORTISOL IN BOYS WITH EARLY-ONSET CONDUCT DISORDER AND CALLOUS-UNEMOTIONAL TRAITS.

BACKGROUND: A growing body of evidence suggests an association between altered hypothalamic-pituitary-adrenal axis reactivity and the development of persistent antisocial behavior in children. However, the effects of altered cortisol levels remain poorly understood in the complex context of conduct disorder, callous-unemotional (CU) personality traits, and frequent comorbidities, such as attention deficit hyperactivity disorder (ADHD). The aim of the current study was to investigate associations among CU traits, antisocial behavior, and comorbid ADHD symptomatology with cortisol levels in male children and adolescents.

METHODS: The study included 37 boys with early-onset conduct disorder (EO-CD, mean age 11.9 years) and 38 healthy boys (mean age 12.5 years). Participants were subjected to multiple daytime salivary cortisol measurements and a psychometric characterization.
RESULTS: Subjects in the EO-CD group with elevated CU traits showed a diminished cortisol awakening response compared to healthy participants. In the EO-CD group, high CU traits and impulsivity were associated with decreased diurnal cortisol levels, while associations with antisocial behavior were not detected. The cortisol awakening response was significantly inversely associated with hyperactivity ($P = 0.02$) and marginally significant with CU traits ($P=0.07$).

CONCLUSIONS: These results indicate a specific association between CU traits and a diminished stress response, which is not explained by antisocial behavior in general.

THE EFFECTIVENESS OF POLICE CUSTODY ASSESSMENTS IN IDENTIFYING SUSPECTS WITH INTELLECTUAL DISABILITIES AND ATTENTION DEFICIT HYPERACTIVITY DISORDER.

Young S, Goodwin EJ, Sedgwick O, et al.

Background: Intellectual Disabilities (ID) and Attention Deficit Hyperactivity Disorder (ADHD) are recognized psychological vulnerabilities in police interviews and court proceedings in England and Wales. The aims of this study were to investigate: (a) the prevalence of ID and/or ADHD among suspects detained at a large London metropolitan police station and their relationship with conduct disorder (CD), (b) the impact of their condition on police staff resources, (c) the effectiveness of current custody assessment tools in identifying psychological vulnerabilities, and (d) the use of 'Appropriate Adults' in interviews.

Method: A total of 200 individuals in a police custody suite were interviewed and screened for ID, ADHD (current symptoms) and CD.

Results: The screening rates for these three disorders were 6.7%, 23.5% and 76.3%, respectively. ADHD contributed significantly to increased requests being made of staff after controlling for CD and duration of time in custody. This is a novel finding. Reading and writing difficulties and mental health problems were often identified from the custody risk assessment tools, but they were not used effectively to inform on the need for the use of an Appropriate Adult. The frequency with which Appropriate Adults were provided to support detainees in police interviews (4.2%) remains almost identical to that found in a similar study conducted 20 years previously.

Conclusions: The current findings suggest that in spite of reforms recently made in custodial settings, procedures may not have had the anticipated impact of improving safeguards for vulnerable suspects. Detainees with ID and ADHD require an Appropriate Adult during police interviews and other formal custody procedures, which they commonly do not currently receive. The findings of the current study suggest this may be due, in large part, to the ineffective use of risk-assessment tools and healthcare professionals, which represent missed opportunities to identify such vulnerabilities.

PARENT-REPORTED SLEEP PROBLEMS, SYMPTOM RATINGS, AND SERUM FERRITIN LEVELS IN CHILDREN WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER: A CASE CONTROL STUDY.

Abou-Khadra MK, Amin OR, Shaker OG, et al.

Background: Sleep problems are common among children with attention-deficit/hyperactivity disorder (ADHD). Serum ferritin levels have been associated with the severity of symptoms and sleep disturbances among children with ADHD. This study was conducted to investigate parent-reported sleep problems in a sample of Egyptian children with ADHD and to examine the relationship between their sleep, symptom-ratings, and low serum ferritin levels.

Methods: Parents of 41 ADHD children, aged 6 to 12 years, filled out the Children's Sleep Habits Questionnaire (CSHQ) and Conners' Parent Rating Scale-Revised: Long Version (CPRS-R:L) in Arabic. Serum ferritin levels were determined with an enzyme-linked immunosorbent assay. The parents of the 62 controls filled out the CSHQ.

Results: The ADHD group showed significantly higher scores in CSHQ subscales and total score. Children with serum ferritin levels <30 ng/mL had more disturbed sleep. There were significant negative correlations between sleep duration subscale, total score of CSHQ, and serum ferritin levels. There were no significant
differences in hyperactivity, cognitive problems/inattention, oppositional, or ADHD index subscale scores between children with serum ferritin levels <30 ng/mL and those with serum ferritin levels (greater-than or equal to)30 ng/mL.

**Conclusions:** Sleep problems are common, and this study suggests an association between low serum ferritin levels and sleep disturbances.

**References:**

BMJ. 2013;347:f6172.

**ATTENTION-DEFICIT/HYPERACTIVITY DISORDER: ARE WE HELPING OR HARMING?**

Thomas R, Mitchell GK, Batstra L.

BMJ (Online). 2013;347.

**ARE CONCERNS ABOUT DSM-5 ADHD CRITERIA SUPPORTED BY EMPIRICAL EVIDENCE?**

Cortese S.


**ADULT ATTENTION-DEFICIT HYPERACTIVITY DISORDER AND OBESITY: EPIDEMIOLOGICAL STUDY.**

Cortese S, Faraone SV, Bernardi S, et al.

BACKGROUND: A significant association between attention-deficit hyperactivity disorder (ADHD) and obesity has been reported. This study addresses unexplored aspects of this relationship.

AIMS: To evaluate the association between adult obesity and: (a) persistent, remitted or lifetime ADHD; (b) number of childhood ADHD symptoms, controlling for socioeconomic status and mood, anxiety and substance use disorders.

METHOD: Face-to-face psychiatric interviews in 34 653 US adults from the National Epidemiologic Study on Alcohol and Related Conditions. Obesity was defined as a body mass index >/=30.

RESULTS: Persistent, lifetime or remitted ADHD were not associated with obesity after controlling for confounders. The number of childhood ADHD symptoms was significantly associated with adult obesity, even after adjustment, in women.

CONCLUSIONS: Childhood ADHD symptoms are associated with obesity in women even after comorbid psychiatric disorders are accounted for. This provides a rationale for longitudinal studies assessing the impact of the treatment of childhood ADHD symptoms on obesity in women.


**NEUROBEHAVIORAL AND HEMODYNAMIC EVALUATION OF STROOP AND REVERSE STROOP INTERFERENCE IN CHILDREN WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.**


Failure of executive function (EF) is a core symptom of attention-deficit/hyperactivity disorder (ADHD). However, various results have been reported and sufficient evidence is lacking. In the present study, we evaluated the characteristics of children with ADHD using the Stroop task (ST) and reverse Stroop task (RST) that reflects the inhibition function of EF. We compared children with ADHD, typically developing children (TDC), and children with autism spectrum disorder (ASD), which is more difficult to discriminate from ADHD. A total of 10 children diagnosed with ADHD, 15 TDC, and 11 children diagnosed with ASD, all matched by age, sex, language ability, and intelligence quotient, participated in this study. While each subject performed computer-based ST and RST with a touch panel, changes in oxygenated hemoglobin (oxy-Hb) were measured in the prefrontal cortex (PFC) by near-infrared spectroscopy (NIRS) to correlate test performance with neural activity. Behavioral performance significantly differed among 3 groups during RST but not during ST. The ADHD group showed greater color interference than the TDC group. In
addition, there was a negative correlation between right lateral PFC (LPFC) activity and the severity of
attention deficit. Children with ADHD exhibit several problems associated with inhibition of color, and this
symptom is affected by low activities of the right LPFC. In addition, it is suggested that low hemodynamic
activities in this area are correlated with ADHD.

MORPHOMETRIC CORRELATION OF IMPULSIVITY IN MEDIAL PREFRONTAL CORTEX.
Impulsivity is a complex behaviour composed of different domains encompassing behavioural dis-inhibition,
risks decision-making and delay discounting abnormalities. To investigate regional brain correlates
between levels of individual impulsivity and grey matter volume, we performed voxel-based morphometric
analysis in 34 young, healthy subjects using impulsivity scores measured with Barratt Impulsivity Scale-11 and computerized Kirby’s delay discounting task. The VBM analysis showed that
impulsivity appears to be reliant on a network of cortical (medial prefrontal cortex and dorsolateral
prefrontal cortex) and subcortical (ventral striatum) structures emphasizing the importance of brain
networks associated with reward related decision-making in daily life as morphological biomarkers for
impulsivity in a normal healthy population. While our results in healthy volunteers may not directly extend to
pathological conditions, they provide an insight into the mechanisms of impulsive behaviour in patients with
abnormalities in prefrontal/frontal-striatal connections, such as in drug abuse, pathological gambling, ADHD
and Parkinson’s disease.

COGNITIVE POTENTIAL OF CHILDREN WITH ATTENTION DEFICIT AND HYPERACTIVITY DISORDER.
Romero AC, Capellini SA, Frizzo AC.
The literature has described comorbidities among the symptoms of children with Attention Deficit and
Hyperactivity Disorder (ADHD) and the auditory processing changes, and these symptoms have been
overlooked in the assessment, and consequently, on the rehabilitation of these individuals. OBJECTIVE:
To compare the findings of the long latency auditory evoked potentials in children with and without ADHD.
METHOD: This is a historical cohort cross-sectional case-control study, in which we enrolled 30 children
with and without ADHD, aged 8-12 years. We performed the long-latency auditory evoked potential test in
two scanning procedures through passive and active tasks differing in frequency and duration (MMNf and
MMNd) (P300f and P300D). RESULTS: When comparing the performance of children with and without
ADHD in the electrophysiological test assessment of hearing, we found significant differences concerning
the P2 amplitude in the LE - which was higher for the ADHD group; and concerning the N2 amplitude and
latency - which were abnormal in the ADHD group. CONCLUSION: This study provided a greater
understanding of the central auditory pathways of children with and without ADHD when evaluated from
electrophysiological tests.

ATtribution PROCesses in Parent–Adolescent conflict in families of adolescents with and without
ADHD.
Markel C, Wiener J.
Parent–Adolescent conflict and attributions for that conflict were examined in a sample of 51 families of 13-
to 17-year-old adolescents with (n = 29) and without (n = 22) attention-deficit/hyperactivity disorder
(ADHD). Adolescents, mothers, and fathers completed questionnaires assessing their conflict and
attributions for their parent–adolescent conflict. Adolescents with ADHD and their parents have conflicts
over more issues than adolescents without ADHD and their parents. Attributions were not predictive of
conflict over and above ADHD status according to adolescent or mother report. Attributions moderated ADHD status in predicting father-reported conflict. Fathers of youth with ADHD who believed conflict was pervasive across contexts and stable over time reported more issues involving conflicts than fathers of youth without ADHD. In addition, fathers of youth with ADHD who believed that conflicts were their sons’ or daughters’ responsibility were less likely to report more issues involving conflict than fathers of youth without ADHD.


VALIDATION D’UN TEST D’INHIBITION AUPRÈS D’ENFANTS PRÉSENTANT UN TROUBLE DÉFICITAIRE DE L’ATTENTION AVEC OU SANS HYPERACTIVITÉ.


The objective of this study was to assess the development of inhibition in 5–11 year-old children with the “Stroop Fruit” task (see Archibald & Kerns, 1999; Catale & Meulemans, 2005) and to examine the clinical value of this tool. Three-hundred forty-six French-speaking children without any developmental disorders or learning disabilities were included in this study. A clinical group of 25 children with attention deficit and hyperactivity disorder was also assessed with this task. Developmental analyses on age groups show an enhancement of performance in the interference condition between 5 and 8 years old. Furthermore, results also show that the clinical group performed significantly less accurately than the control group for the interference condition, which confirms the clinical interest of this tool.


COGNITIVE AND BEHAVIORAL ATTENTION IN CHILDREN WITH MATH DIFFICULTIES.


Cognitive assessments and behavioral ratings of attention were used to examine the relation of inattention to math performance in children. Third grade students with math difficulties (MD; n=17) and math and reading difficulties (MDRD; n=35) were administered the Attentional Network Test (ANT), as well as achievement and intelligence measures. Strengths and Weaknesses of ADHD-Symptoms and Normal-Behavior-IV (SWAN-IV) Inattention ratings were collected from teachers. Two comparison groups were also recruited: a typically achieving group (n=23) and a group that responded to a math-tutoring intervention (responders; n=54). On the ANT, children with MD and MDRD did not perform significantly different than typically achieving children or responders on measures of alerting and orienting attention and executive control. All subgroups did demonstrate performance patterns that were expected on the ANT. However, performance across blocks of the task was inconsistent, suggesting poor reliability. There were no relations between ANT performance and SWAN-IV behavioral inattention scores, though behavioral ratings of inattention correlated significantly with math performance. Children with MD and MDRD may have more difficulty with distraction and attention to detail in contextual situations, as opposed to impulsive responding in these settings. The lack of relation between cognitive attention and math performance may suggest that either the ANT does not assess the relevant attention constructs associated with math difficulties or may parallel studies of attention deficit/hyperactivity disorder (ADHD) in which cognitive and behavioral assessments are weakly related.


NEUROPSYCHOLOGICAL IMPAIRMENTS ON THE NEPSY-II AMONG CHILDREN WITH FASD.


BACKGROUND: We examined the pattern of neuropsychological impairments of children with FASD (compared to controls) on NEPSY-II measures of attention and executive functioning, language, memory, visuospatial processing, and social perception.
METHODS: Participants included 32 children with FASD and 30 typically developing control children, ranging in age from 6 to 16 years. Children were tested on the following subtests of the NEPSY-II: Attention and Executive Functioning (animal sorting, auditory attention/response set, and inhibition), Language (comprehension of instructions and speeded naming), Memory (memory for names/delayed memory for names), Visual-Spatial Processing (arrows), and Social Perception (theory of mind). Groups were compared using MANOVA.

RESULTS: Children with FASD were impaired relative to controls on the following subtests: animal sorting, response set, inhibition (naming and switching conditions), comprehension of instructions, speeded naming, and memory for names total and delayed, but group differences were not significant on auditory attention, inhibition (inhibition condition), arrows, and theory of mind. Among the FASD group, IQ scores were not correlated with performance on the NEPSY-II subtests, and there were no significant differences between those with and without comorbid ADHD.

CONCLUSIONS: The NEPSY-II is an effective and useful tool for measuring a variety of neuropsychological impairments among children with FASD. Children with FASD displayed a pattern of results with impairments (relative to controls) on measures of executive functioning (set shifting, concept formation, and inhibition), language, and memory, and relative strengths on measures of basic attention, visual spatial processing, and social perception.

Prevalence of emotional and behavioral symptoms and their impact on daily life activities in a community sample of 3 to 5-year-old children.


The aim of the study was to evaluate prevalence and impact of behavioral/emotional symptoms in preschoolers. The sample comprised 1,738 preschoolers with an age range between 37 and 63 months. Parents rated children’s symptoms using the Strengths and Difficulties Questionnaire (SDQ) and the impact of perceived difficulties using the impact supplement of the SDQ. The prevalence of a total difficulties score in an abnormal/borderline range was 16.0% that means lower than rates in schoolchildren. 8.6% of the preschoolers were rated as symptomatic (borderline/abnormal) and their symptoms were rated as having some or considerable impact on their lives. Parents mostly reported problems of hyperactivity/inattention and their interference with learning abilities. All symptoms scales of the SDQ, except prosocial behavior, significantly explained impact of perceived difficulties. Parents of boys rated significantly higher levels of symptoms and impact. Low parental education was associated with more symptoms and higher impact.

Childhood obesity: a review of increased risk for physical and psychological comorbidities.

Pulgaron ER.

BACKGROUND: Worldwide estimates of childhood overweight and obesity are as high as 43 million, and rates continue to increase each year. Researchers have taken interest in the childhood obesity epidemic and the impact of this condition across health domains. The consequences of childhood and adolescent obesity are extensive, including both medical and psychosocial comorbidities.

OBJECTIVE: The purpose of this review was to consolidate and highlight the recent literature on the comorbidities associated with childhood obesity, both nationally and internationally.

METHODS: PubMed and PsychINFO searches were conducted on childhood obesity and comorbidities.

RESULTS: The initial search of the terms obesity and comorbidity yielded >5000 published articles. Limits were set to include studies on children and adolescents that were published in peer-reviewed journals from 2002 to 2012. These limits narrowed the search to 938. Review of those articles resulted in 79 that are included in this review. The major medical comorbidities associated with childhood obesity in the current literature are metabolic risk factors, asthma, and dental health issues. Major psychological comorbidities include internalizing and externalizing disorders, attention-deficit hyperactivity disorder, and sleep problems.
CONCLUSIONS: The high prevalence rates of childhood obesity have resulted in extensive research in this area. Limitations to the current childhood obesity literature include differential definitions of weight status and cut-off levels for metabolic risk factors across studies. Additionally, some results are based on self-report of diagnoses rather than chart reviews or physician diagnosis. Even so, there is substantial support for metabolic risk factors, internalizing disorders, attention-deficit hyperactivity disorder, and decreased health-related quality of life as comorbidities to obesity in childhood. Additional investigations on other diseases and conditions that might be associated with childhood obesity are warranted and intervention research in this area is critical.


**TOURETTE DISORDER TREATED WITH VALPROIC ACID.**

Ye L, Lippmann S.

Valproic acid was successfully prescribed for a 10-year old boy suffering from Tourette's Disorder with a co-morbid bipolar diagnosis. Valproic acid has demonstrated efficacy in reducing the total number of motorics, their frequency, intensity, complexity, and impairment in a patient who had failed to respond to numerous other medications. Valproic acid may be a useful agent to consider for children with treatment-resistant Tourette's disorder.


**SELF-ESTEEM REACTIVITY AMONG MOTHERS OF CHILDREN WITH ATTENTION-DEFICIT/ HYPERACTIVITY DISORDER: THE MODERATING ROLE OF DEPRESSION HISTORY.**


This study examined self-esteem reactivity to a variety of contextual cues in a sample of women prone to depression. Participants were 49 mothers of children with attention-deficit/hyperactivity disorder. Across a 9-month time-period, participants completed weekly measures of self-esteem, perceived stress, positive and negative affect, and child disruptive behavior. Results indicated that mothers reported lower self-esteem during weeks they experienced greater stress, lower positive affect, higher negative affect, and more inattentive, overactive, and oppositional behavior in their children. Depression history moderated these relationships such that mothers with prior histories of depression reported greater self-esteem reactivity to these cues than never depressed mothers.


**THE COMORBIDITY OF ADULT ATTENTION-DEFICIT/HYPERACTIVITY DISORDER IN BIPOLAR DISORDER PATIENTS.**

Karaahmet E, Konuk N, Dalkilic A, et al.

**OBJECTIVE:** High comorbidity ratio of bipolar mood disorder (BMD) with Axis I and Axis II diagnoses is reported in the literature. The possible relationship between BMD and attention-deficit/hyperactivity disorder (ADHD) in all age groups has been attracting more attention of researchers due to highly overlapping symptoms such as excessive talking, attention deficit, and increased motor activity. In this study, we aimed to investigate the prevalence of ADHD comorbidity in BMD patients and the clinical features of these patients.

**METHODS:** Of 142 patients, who presented to the Bipolar Disorder Unit of Zonguldak Karaelmas University Research and Application Hospital between the dates of August 1, 2008 and June 31, 2009 and diagnosed with BMD according to DSM-IV criteria consecutively, 118 patients signed informed consent and 90 of them completed the study. They all were in euthymic phase during the study evaluations. A sociodemographical data form, Wender-Utah Rating Scale (WURS), ADD/ADHD Diagnostic and Evaluation Inventory for Adults, and Structural Clinical Interview for DSM-IV Axis I Disorders, Clinical Version (SCID-I) were applied to all participating patients.
RESULTS: A total of 23.3% of all patients met the criteria for A-ADHD diagnosis along BMD. No difference was detected regarding sociodemographical features between the BMD+A-ADHD and the BMD without A-ADHD groups. The BMD+A-ADHD group had at least one extra educational year repetition than the other group and the difference was statistically significant. The BMD starting age in the BMD+A-ADHD group was significantly earlier (p=0.044) and the number of manic episodes was more frequent in the BMD+A-ADHD group (p=0.026) than the BMD without ADHD group. Panic disorder in the BMD+A-ADHD group (p=0.019) and obsessive-compulsive disorder in the BMD+C-ADHD group (p=0.001) were most frequent comorbidities.

CONCLUSIONS: A-ADHD is a frequent comorbidity in BMD. It is associated with early starting age of BMD, higher number of manic episodes during the course of BMD, and more comorbid Axis I diagnoses.

LIFE EVENTS AND TOURETTE SYNDROME.
Steinberg T, Shmuel-Baruch S, Horesh N, et al.

INTRODUCTION: Tourette syndrome (TS) is a neuropsychiatric developmental disorder characterized by the presence of multiple motor tics and one or more vocal tics. Although TS is primarily biological in origin, stress-diatheses interactions most probably play a role in the course of the illness. The precise influence of the environment on this basically biological disorder is difficult to ascertain, particularly when TS is complicated by comorbidities. Among the many questions that remain unresolved are the differential impact of positive and negative events and specific subtypes of events, and the importance of major crucial events relative to minor daily ones to tic severity.

OBJECTIVES: To examine the relationships between life events, tic severity and comorbid disorders in Tourette Syndrome (TS), including OCD, ADHD, anxiety, depression and rage attacks. Life events were classified by quantity, quality (positive or negative) and classification types of events (family, friends etc.).

SUBJECTS: Sixty patients aged 7-17 years with Tourette syndrome or a chronic tic disorder were recruited from Psychological Medicine Clinic in Schneider Children's Medical Center of Israel.

INSTRUMENTS: Yale Global Tic Severity Scale; Children's Yale Brown Obsessive Compulsive Scale; Life Experiences Survey; Brief Adolescent Life Events Scale; Screen for Child Anxiety Related Emotional Disorders; Child Depression Inventory/Beck Depression Inventory; ADHD Rating Scale IV; Overt Aggression Scale.

RESULTS: Regarding tics and minor life events, there was a weak but significant correlation between severity of motor tics and the quantity of negative events. No significant correlation was found between tic severity and quantity of positive events. Analysis of the BALES categories yielded a significant direct correlation between severity of vocal tics and quantity of negative events involving friends. Regarding comorbidities and minor life events, highly significant correlations were found with depression and anxiety. Regarding tics and major life events, significant correlation was found between the quantity of major life events and the severity of motor tics, but not vocal tics. Regarding comorbidities and major life events, significant correlation was found between the severity of compulsions, ADHD, and aggression and the subjects' personal evaluation of the effect of negative major life events on their lives.

CONCLUSIONS: Minor life events appear to be correlated with tic severity and comorbidities in children and adolescents with Tourette syndrome. The lack of an association between major life events and tic severity further emphasizes the salient impact of minor life events that occur in temporal proximity to the assessment of tic severity. Clinically, the results match our impression from patient narratives wherein they "blamed" the exacerbations in tics on social interactions. The high correlation between negative life events and depression, anxiety and compulsions symptoms, were reported also in previous studies. In conclusion, These findings may have clinical implications for planning supportive psychotherapy or cognitive behavioral therapy for this patient population.
RISK FACTORS FOR SECONDARY SUBSTANCE USE DISORDERS IN PEOPLE WITH CHILDHOOD AND ADOLESCENT-ONSET BIPOLAR DISORDER: OPPORTUNITIES FOR PREVENTION.

Kenneson A, Funderburk JS, Maisto SA.

BACKGROUND: Compared to other mental illnesses, bipolar disorder is associated with a disproportionately high rate of substance use disorders (SUDs), and the co-occurrence is associated with significant morbidity and mortality. Early diagnosis of primary bipolar disorder may provide opportunities for SUD prevention, but little is known about the risk factors for secondary SUD among individuals with bipolar disorder. The purposes of this study were to describe the population of people with childhood and adolescent-onset primary bipolar disorder, and to identify risk factors for secondary SUD in this population.

METHODS: Using data collected from the National Comorbidity Survey Replication study, we identified 158 individuals with childhood-onset (<13 years) or adolescent-onset (13-18 years) primary bipolar disorder (I, II or subthreshold). Survival analysis was used to identify risk factors for SUD.

RESULTS: Compared to adolescent-onset, people with childhood-onset bipolar disorder had increased likelihoods of attention deficit hyperactivity disorder (ADHD) (adjusted odds ratio=2.81) and suicide attempt (aOR=3.61). Males were more likely than females to develop SUD, and did so at a faster rate. Hazard ratios of risk factors for SUD were: lifetime oppositional defiant disorder (2.04), any lifetime anxiety disorder (3.077), adolescent-onset bipolar disorder (1.653), and suicide attempt (15.424). SUD was not predicted by bipolar disorder type, family history of bipolar disorder, hospitalization for a mood episode, ADHD or conduct disorder.

CONCLUSIONS: As clinicians struggle to help individuals with bipolar disorder, this study provides information that might be useful in identifying individuals at higher risk for SUD. Future research can examine whether targeting these risk factors may help prevent secondary SUD.

THE ASSOCIATION OF EARLY PARENT SUPPORT FOR CHILD AUTONOMY WITH CHANGES IN BULLYING AMONG CHILDREN WITH AND WITHOUT ADHD AND ODD.

Kruszewski E, Rajendran K, Halperin JM.

Background: Bullying is more prevalent among children with attention-deficit/hyperactivity disorder (ADHD) and/or oppositional-defiant disorder (ODD) than among children without these disorders. Children of authoritative parents who support the child’s autonomy have a lower risk for bullying. However, it is not clear whether parent support for child autonomy (PSA) influences changes in bullying over time among ADHD children with and without comorbid ODD relative to those without these disorders.

Methods: We prospectively examined 162 children from the New York metropolitan area (115 boys) over 5 assessment points (T1-T5) between the ages of 5 and 9 years. Bullying was measured at T1-T5 using an aggregate of three items (bullies others; threatens to hurt others; teases others) rated by teachers on a 4-point scale. Child diagnoses (Neither ADHD nor ODD, ADHD but not ODD, both ADHD and ODD) were assessed using parent interviews on the Kiddie-SADS. PSA was assessed at T1 by conducting laboratory observations and coding parent behaviors using the Coding System for Mother-Child Interactions, respectively.

Results: There were no gender differences in bullying (T1-T5). Lower SES was associated with greater bulling and was included as a covariate. Children with ADHD + ODD (N = 32) were significantly more likely to bully than those with no diagnosis (N = 89) at all time points; and more likely to bully than those who had ADHD without ODD (N = 41) at T1 and T4. Hierarchical linear modeling showed a significant fall in bullying over five-years [B(SE) = -.12(.04), p = .001]. Diagnostic status was associated with the initial level [B(SE) = 1.28(.35), p = .001] and marginally with change in bullying [B(SE) = -.10(.05), p = .05], with a greater fall among those with ADHD + ODD. PSA was not associated with initial levels of bullying, but was associated with a reduction in bullying over time [B(SE) = -.16(.07), p = .03]. Irrespective of group, children receiving high PSA had a greater decline in bullying than those with low PSA.

Conclusion: Interventions that enhance PSA during early school-age may lower the risk for later bullying.
ADHD AND MOTOR CONTROL: A REVIEW OF THE MOTOR CONTROL DEFICIENCIES ASSOCIATED WITH ATTENTION DEFICIT/HYPERACTIVITY DISORDER AND CURRENT TREATMENT OPTIONS.
Demers MM, McNevin N, Azar N.
A common trait in individuals with attention deficit/hyperactivity disorder (ADHD) is reduced motor control and function; studies have found motor control deficiencies in 30-50% of children with ADHD, depending on the method of measurement. Studies have documented several notable differences in the brains of individuals with ADHD compared to age-matched controls, most of which are in areas responsible for executive and motor control. Differences have been observed in the prefrontal cortex, the frontostriatal region, and the cerebellum. The current literature indicates that individuals with ADHD have increased movement variability and decreased movement accuracy; however, movement speed does not seem to be affected. Motor control deficiencies are prominent among individuals with ADHD, yet few treatment options are available. Current research indicates that the use of an external sensory stimulus can reduce the motor control deficiencies seen in children and adolescents with ADHD.

HEALTHCARE REFORM, QUALITY, AND TECHNOLOGY: ADHD AS A CASE STUDY.
Baum RA, Epstein JN, Kelleher K.
The concepts of healthcare reform and population health are shifting the emphasis from traditional, volume-based care to a model in which value, or quality, predominates. High quality care will be increasingly rewarded, with financial consequences for poor performance. This shift will be accelerated by the use of healthcare technology, a rapidly growing industry with tools ranging from electronic health records to smart phones and web portals. In this article we highlight pertinent legislative reforms followed by a review of technologies that may play a role in the implementation of these reforms. Pediatric Attention Deficit Hyperactivity Disorder is used as an example given the large number of proposed tools for this condition. While the evidence base is weak for some technologies, research regarding web portals is better developed and will be presented as an example of a technology that may allow practitioners and organizations to improve healthcare quality in several dimensions.

THE COMORBIDITY OF ADHD AND BIPOLAR DISORDER: ANY LESS CONFUSION?
Pataki C, Carlson GA.
The clinical confusion surrounding childhood ADHD and bipolar disorder centers on overlaps between severe ADHD with mood lability and mania/hypomania. Perplexity has been exacerbated by the removal of mood symptoms from the diagnostic criteria for ADHD and a lack of stringent criteria for a manic/hypomanic episode. This review summarizes current knowledge of the relationship between ADHD and bipolar disorder, the rates with which ADHD and bipolar disorder coexist in youth of differing ages, their presence in community, clinical, and high risk samples, and their longitudinal course. Treatment studies are reviewed, highlighting findings in comorbid cases, which support the efficacy of stimulants and other agents for ADHD without worsening mood symptoms, and efficacy of second generation antipsychotics for bipolar disorder. In conclusion, a lack of clarity regarding the diagnostic boundaries between childhood ADHD and bipolar disorder remains, however, treatments targeting symptoms of each disorder when comorbid, provide some efficacy.
FAMILY FUNCTION AND ITS RELATIONSHIP TO INJURY SEVERITY AND PSYCHIATRIC OUTCOME IN CHILDREN WITH ACQUIRED BRAIN INJURY: A SYSTEMATIZED REVIEW.
Lax Pericall MT, Taylor E.

AIM: The psychological and psychiatric outcome of children with acquired brain injury is influenced by many variables. A review was undertaken to clarify the contribution of family function, how it relates to injury severity, and what particular aspects of family function influence psychological outcome in this group.

METHOD: A systematized review of the literature of studies published between 1970 and 2012 from OvidMedline, PsychInfo, PsycARTICLES, and Cochrane was undertaken focusing on family function, injury severity, and psychiatric outcome.

RESULTS: Thirty-six papers met the inclusion criteria. Injury severity was linked to the development of organic personality change. Family function before injury, measured by the Family Assessment Device or the Clinical Rating Scale, had a statistically significant effect on general psychological functioning in six out of eight studies. Family function had a significant effect for oppositional defiant disorder and secondary attention-deficit-hyperactivity disorder. The effects of family function may differ depending on the age of the child and the severity of the injury. Some styles of parenting moderated recovery. After injury, family function was related to the child’s contemporaneous psychiatric symptoms. The level of evidence for these papers was 3 or 4 (Oxford Centre for Evidence-based Medicine criteria).

INTERPRETATION: Screening for some aspects of family functioning before injury and family function during the rehabilitation phase may identify children at risk of psychiatric disorders.

GENE-ENVIRONMENT INTERACTION BETWEEN DOPAMINE RECEPTOR D4 7-REPEAT POLYMORPHISM AND EARLY MATERNAL SENSITIVITY PREDICTS INATTENTION TRAJECTORIES ACROSS MIDDLE CHILDHOOD.
Berry D, Deater-Deckard K, McCartney K, et al.

Evidence suggests that the 7-repeat variant of a 48 base pair variable number tandem repeat polymorphism in the dopamine receptor D4 (DRD4) gene may be associated with the development of attention problems. A parallel literature suggests that genes linked to dopaminergic functioning may be associated with differential sensitivity to context, such that the direction of the genetic effect is hypothesized to vary across environmental experience. Guided by these literatures, we used data from the NICHD Study of Early Child Care and Youth Development to consider (a) whether individual differences in children's inattention problems across middle childhood are predicted by gene-environment interactions between the DRD4 gene 7-repeat polymorphism and children’s experiences of maternal sensitivity across infancy and early childhood and (b) the degree to which such interactions are consistent with the differential-sensitivity model. Largely consistent with the hypothesized model, gene-environment interactions indicated that, in the context of insensitive early maternal care, the DRD4 7-repeat polymorphism was associated with higher levels of inattention. Although somewhat less consistently, there was also evidence that, in the context of highly sensitive early maternal care, the 7-repeat polymorphism was associated with lower levels of inattention. Overall, the magnitude of the absolute genetic effect increased over time, as children's inattention trajectories diverged.

ATTENTION DEFICIT HYPERACTIVITY DISORDER (ADHD) IMPACTS DIABETES MANAGEMENT AND GLYCEMIC CONTROL AMONG ADOLESCENTS AND YOUNG ADULTS WITH TYPE 1 DIABETES (T1D).

This analysis assesses the effect of ADHD on T1D management and glycemic control among 4,540 adolescents and young adults, ages 13-26 yrs, participating in the T1D Exchange clinic registry (median age 16.7 yrs, duration 7.0 yrs, 49% female, 82% white). Participants (pts) were classified as ADHD not on medication (meds), ADHD on meds, or no ADHD. Groups were compared in logistic and linear regression models for: self-monitoring of blood glucose (SMBG) /day, missed insulin dose (greater-than or equal to)1
time/week, HbA1c, and diabetic ketoacidosis (DKA) and severe hypoglycemic (SH) events in the past 3 months. Overall, 460 (10%) pts reported a diagnosis of ADHD of whom 51% (235) currently took meds. Mean SMBG/day was 4.5, 4.9, and 5.0 in the ADHD not on meds, ADHD on meds, and no ADHD groups, respectively (P=0.17). ADHD pts on meds (41%, P<0.001) or not (38%, P=0.003) were more likely to report missing insulin doses compared with no ADHD pts (30%). Mean HbA1c was higher in ADHD not on meds (9.0%, P=0.003) but not ADHD on meds (8.7%, P=0.06) compared with no ADHD pts (8.6%). Frequency of SH was higher among ADHD not on meds (P=0.001) but not ADHD on meds (P=0.19) compared with no ADHD, whereas DKA frequency was higher for ADHD not on meds (P=0.01) and on meds (P=0.04) compared with no ADHD (Figure). ADHD adversely affects diabetes management and clinical outcomes. T1D outcomes in patients with ADHD, with and without treatment, should be further assessed. (Figure Presented).

SIMULTANEOUS USE OF NON-MEDICAL ADHD PRESCRIPTION STIMULANTS AND ALCOHOL AMONG UNDERGRADUATE STUDENTS.
Egan KL, Reboussin BA, Blocker JN, et al.
BACKGROUND: Use of prescription stimulants used to treat Attention Deficit/Hyperactivity Disorder (ADHD) for reasons other than prescribed, known as non-medical use, is a growing problem among undergraduates. Previous studies show that non-medical prescription stimulant (NMPS) users consume more alcohol than individuals who do not use NMPS. However, research on simultaneous use of NMPS and alcohol is limited. The objectives of this study were to: (1) determine the prevalence of simultaneous use of alcohol and NMPS; (2) examine predictors and consequences of simultaneous NMPS and alcohol use among undergraduates.
METHODS: In fall 2009, 4090 students from eight North Carolina universities completed a web-based survey.
RESULTS: Past year prevalence of NMPS use among this sample was 10.6% and simultaneous use of NMPS with alcohol was 4.9%. Among NMPS users, 46.4% used NMPS simultaneously with alcohol within the past year. Multivariable analysis revealed that simultaneous NMPS and alcohol use was associated with low grade point averages, use of other substances, and increased alcohol-related consequences. Simultaneous NMPS and alcohol users reported experiencing significantly more negative consequences than either past year drinkers who did not use prescription stimulants and concurrent NMPS and alcohol users (use over the past year but not at the same time).
CONCLUSIONS: Simultaneous use of NMPS and alcohol is high among NMPS users in our sample of undergraduate students. Simultaneous users are at increased risk of experiencing negative consequences. Thus, prevention and intervention efforts should include a focus on simultaneous NMPS and alcohol use.

IMPULSIVITY AND NEGATIVE MOOD IN ADOLESCENTS WITH LOSS OF CONTROL EATING AND ADHD SYMPTOMS: AN EXPERIMENTAL STUDY.
Hartmann AS, Rief W, Hilbert A.
The aim of the study was to experimentally examine the reactivity of mood and impulsivity to negative mood induction in adolescents with loss of control (LOC) eating and adolescents with attention deficit hyperactivity disorder (ADHD) symptoms. The study included eighty-eight adolescents with LOC eating, ADHD symptoms, and control. Participants self-reported on mood and participated in a stop signal task before and after negative mood induction with Cyberball. Groups did not differ in impulsivity at baseline (p >.05). The LOC group presented with greater increase of negative mood than the ADHD group, and with greater increase of impulsivity than both other groups from pre- to post-Cyberball (p <.05). Stronger reactivity of negative mood and impulsivity in LOC eating corroborates findings in adults that the concepts' association might be specific to binge eating disorder. Additionally, findings add to previous results showing
emotion regulation deficits in LOC eating. Future research should examine the concepts’ impact on actual eating behavior including binge eating.

TRAFFIC-RELATED AIR POLLUTION EXPOSURE IN THE FIRST YEAR OF LIFE AND BEHAVIORAL SCORES AT 7 YEARS OF AGE.
BACKGROUND: There is increasing concern about the potential effects of traffic-related air pollution (TRAP) on the developing brain. The impact of TRAP exposure on childhood behavior is not fully understood because of limited epidemiologic studies.
OBJECTIVE: We explored the association between early-life exposure to TRAP using a surrogate, elemental carbon attributed to traffic (ECAT), and attention deficit/hyperactivity disorder (ADHD) symptoms at 7 years of age.
METHODS: From the Cincinnati Childhood Allergy and Air Pollution Study (CCAAPS) birth cohort we collected data on exposure to ECAT during infancy and behavioral scores at 7 years of age. Children enrolled in CCAAPS had at least one atopic parent and a birth residence either < 400 m or > 1,500 m from a major highway. Children were followed from infancy through 7 years of age. ECAT exposure during the first year of life was estimated based on measurements from 27 air sampling sites and land use regression modeling. Parents completed the Behavioral Assessment System for Children, 2nd Edition, when the child was 7 years of age. ADHD-related symptoms were assessed using the Hyperactivity, Attention Problems, Aggression, Conduct Problems, and Atypicality subscales.
RESULTS: Exposure to the highest tertile of ECAT during the child's first year of life was significantly associated with Hyperactivity T-scores in the "at risk" range at 7 years of age, after adjustment [adjusted odds ratio (aOR) = 1.7; 95% CI: 1.0, 2.7]. Stratification by maternal education revealed a stronger association in children whose mothers had higher education (aOR = 2.3; 95% CI: 1.3, 4.1).
CONCLUSIONS: ECAT exposure during infancy was associated with higher Hyperactivity scores in children; this association was limited to children whose mothers had more than a high school education.

Epilepsy Behav. 2013 Jul;28:41-46.
HYPERACTIVE BEHAVIOR IN A FAMILY WITH AUTOSOMAL DOMINANT LATERAL TEMPORAL LOBE EPILEPSY CAUSED BY A MUTATION IN THE LGI1/EPITEMPIN GENE.
Berghuis B, Brilstra EH, Lindhout D, et al.
Autosomal dominant lateral temporal lobe epilepsy (ADLTE) is characterized by focal seizures with auditory features or aphasia. Mutations in the leucine-rich glioma-inactivated 1 (LGI1) gene have been reported in up to 50% of families with ADLTE. Attention-deficit/hyperactivity disorder (ADHD) symptoms have not yet been reported in these families. Clinical data were collected from a family with five affected members. Leucine-rich glioma-inactivated 1 exons and boundaries were sequenced by standard methods. Attention-deficit/hyperactivity disorder symptoms were scored based on the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV) criteria. Affected members had seizures with auditory features and psychic auras, and some experienced nightmares. A heterozygous c.431+1G>A substitution in LGI1 was detected in all members. Significantly more hyperactivity symptoms were found in family members carrying the LGI1 mutation. This study expands the phenotypic spectrum associated with ADLTE due to LGI1 mutation and underlines the need for more systematic evaluation of ADHD and related symptoms.
**VARIABLE BEHAVIOURAL PHENOTYPES OF PATIENTS WITH MONOSOMIES OF 15q26 AND A REVIEW OF 16 CASES.**


Patients with trisomy or tetrasomy of distal 15q show a recognizable overgrowth syndrome, whereas patients with a monosomy of 15q26 share some degree of pre- and postnatal growth retardation, but differ with respect to facial and skeletal dysmorphisms, congenital heart disease and intellectual development. By reviewing 16 cases with losses of 15q26 we found that the size of the deletion was also not a predictor of the breadth of the phenotypic spectrum, the severity of disease or prognosis of the patient. Although monosomies of 15q26 do not represent a classical contiguous gene syndrome, a few candidate genes for selected features such as proportional growth retardation and cardiac abnormalities have been identified. In 11 out of 16 patients with monosomy of distal 15q variable neurobehavioral phenotypes, including learning difficulties, seizures, attention-deficit-hyperactivity disorder, hearing loss and autism, have been found. We discuss clinical ramifications for cases with a loss of 15q26 detected by prenatal array-CGH.

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**IS ADHD SEVERITY IN ADULTS ASSOCIATED WITH THE LIFETIME PREVALENCE OF COMORBID DEPRESSIVE EPISODES AND ANXIETY DISORDERS?**

Simon V, Czobor P, Bitter I.

**PURPOSE:** The objective of the present study was to examine the association between ADHD severity and the lifetime prevalence of comorbid depressive episodes and anxiety disorders in adults with ADHD.

**SUBJECTS/MATERIALS AND METHODS:** Analyses were based on data of the Conner's Adult ADHD Rating Scale (CAARS) and a parent study examining the epidemiology of adult ADHD in 17 GP practices in Budapest, Hungary. Subjects between 18 and 60 years were included in the screening phase (n=3529). Out of 279 positively screened subjects 161 participated in a clinical interview and completed the CAARS to confirm the diagnosis. We applied four diagnostic criteria: "DSM-IV"; "No-onset" (DSM-IV criteria without the specific requirement for onset); "Symptoms-only" (DSM-IV symptom criterion only); and "Reduced symptoms-only" (DSM-IV symptom criterion with a reduced threshold for symptom count). The MINI PLUS 5.0 was used to assess psychiatric comorbidity.

**RESULTS:** ADHD severity, as measured by the CAARS ADHD Index, showed a significant positive association with the prevalence of comorbid depressive episodes in all but the "ADHD_No-onset" group ("DSM-IV": F[1.23]=8.39, P=0.0081; "No-onset": F(1.27)=0.97, P=0.3346; "Symptoms-only": F[1.55]=30.79, P<0.0001; "Reduced symptoms-only": F(1.62)=26.69, P<0.0001).

**DISCUSSION AND CONCLUSION:** Results indicate that ADHD symptom severity increases in association with lifetime comorbidity with depression.

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**PARENT PREFERENCES REGARDING STIMULANT THERAPIES FOR ADHD: A COMPARISON ACROSS SIX EUROPEAN COUNTRIES.**


The objective is to identify attributes of ADHD stimulant medications that influence treatment preferences of parents of children and adolescents with ADHD across six European countries, using a discrete choice experiment (DCE). Different attributes (and associated levels) of stimulant therapies were identified through literature review and clinician input. Attributes included duration and degree of symptom control after each dose, frequency of medication dosing, potential for treatment to be abused, the side effects of vomiting, loss of appetite, and sleep disturbance. Attributes and levels were combined using an orthogonal design to produce a number of discrete hypothetical treatments. Parents were recruited via patient panels in different countries and asked to complete a survey. DCE data were analyzed using conditional logit models to explore the impact of each attribute on participants' choices. Six hundred individuals (220 parents of adolescents and 380 parents of children) participated. All attributes were significant predictors of choice (p < 0.01). 'Degree of symptom control' was the most important attribute whereby the odds of choosing 'very
much improved symptoms' compared with 'minimally improved' was 4.85 [95% confidence interval (CI) = 4.28-5.49] for the adolescent group and 6.37 (95% CI = 5.79-7.01) for the child group. Some inter-country differences emerged, e.g., achieving the best degree of symptom control was more important to parents in some countries than others. In conclusion, the study showed that duration and degree of symptom control were the most important aspects of treatment for parents in all countries. The findings revealed cultural differences in the relative importance of attributes.

ARE PARENTAL AUTISM SPECTRUM DISORDER AND/OR ATTENTION-DEFICIT/ HYPERACTIVITY DISORDER SYMPTOMS RELATED TO PARENTING STYLES IN FAMILIES WITH ASD (+ADHD) AFFECTED CHILDREN?
Van Steijn DJ, Oerlemans AM, De Ruiter SW, et al.
An understudied and sensitive topic nowadays is that even subthreshold symptoms of autism spectrum disorder (ASD) and attention-deficit/Hyperactivity disorder (ADHD) in parents may relate to their parenting styles. The aim of this study was to explore the influence of (the combined) effect of child diagnosis (ASD or ASD + ADHD affected/unaffected children) and parental ASD and/or ADHD on parenting styles. Ninety-six families were recruited with one child with a clinical ASD (+ADHD) diagnosis, and one unaffected sibling. Parental ASD and ADHD symptoms were assessed using self-report. The Parenting Styles Dimensions Questionnaire (PSDQ) self and spouse-report were used to measure the authoritative, authoritarian, and permissive parenting styles. Fathers and mothers scored significantly higher than the norm data of the PSDQ on the permissive style regarding affected children, and lower on the authoritative and authoritarian parenting style for affected and unaffected children. Self- and spouse-report correlated modestly too strongly. Higher levels of paternal (not maternal) ADHD symptoms were suboptimally related to the three parenting styles. Further, two parent-child pathology interaction effects were found, indicating that fathers with high ADHD symptoms and mothers with high ASD symptoms reported to use a more permissive parenting style only towards their unaffected child. The results highlight the negative effects of paternal ADHD symptoms on parenting styles within families with ASD (+ADHD) affected offspring and the higher permissiveness towards unaffected offspring specifically when paternal ADHD and/or maternal ASD symptoms are high. Parenting training in these families may be beneficial for the well-being of all family members.

COMMON DANISH STANDARDS IN PRESCRIBING MEDICATION FOR CHILDREN AND ADOLESCENTS WITH ADHD.
Assessing whether symptoms of attention-deficit hyperactivity disorder (ADHD) in children are age-inappropriate is essential. Hence, comparing children within one school grade is problematic and the risk of applying relative standards is inherent. Being young-for-grade increases the likelihood of receiving medication in countries with high prevalence of ADHD medication. We test the same hypothesis in a cohort of 418,396 children and find no difference between children who are young-for-grade and old-for-grade. The Danish system, with its restrictive approach to medication and clear diagnostic guidelines seems to have avoided a systematic bias of ADHD medication in young children reported in other countries.

DIFFERENTIAL EFFECTS OF ANXIETY AND DEPRESSIVE SYMPTOMS ON WORKING MEMORY COMPONENTS IN CHILDREN AND ADOLESCENTS WITH ADHD COMBINED TYPE AND ADHD INATTENTIVE TYPE.
Ferrin M, Vance A.
Working memory (WM) deficits have been shown to be associated with core ADHD symptoms, worse academic achievement and peer-relationship problems. Internalizing symptoms, such as anxiety and depression, have also been associated with impaired WM performance. However, the association of
anxiety and depression and WM performance remains unclear for children and adolescents with ADHD. Further, it is unknown how these comorbid conditions might affect WM performance in the two main ADHD subtypes. The association of anxiety and depression and the specific components of spatial (SWM) and verbal working memory (VWM) were examined in 303 children and adolescents with ADHD, combined type (ADHD-CT) and 77 ADHD, inattentive type (ADHD-IA) compared to 128 age- and gender-matched typically developing participants. The relationship between anxiety and depression and WM was assessed using multiple linear regression analyses and separate simple regression analyses. Higher levels of anxiety/depression were associated with (1) increased between-search errors in the typically developing participants alone, (2) a better strategy performance in the ADHD-CT group, and (3) a better spatial span performance in the ADHD-IA group. VWM was equally impaired in the ADHD-CT and ADHD-IA groups, independent of the levels of anxiety and depression. The results suggest that the effects of internalizing symptoms on WM differ in typically developing children and adolescents compared to those with ADHD. Further, high levels of anxiety and depression modified WM performance differently according to the specific ADHD subtypes. This might help explain contradictory findings observed in previous studies of mixed samples of participants with ADHD-CT and ADHD-IA.


Methylphenidate (MPH) is the first choice of medical treatment for attention-deficit/hyperactivity disorder (ADHD). Its mechanism of action is to inhibit the reuptake of dopamine and noradrenaline mainly in the region of the striatum. It has been estimated that 10-30 % of patients with ADHD do not respond adequately to MPH. The aim of this study was to evaluate whether striatal differences exist between good and poor responders to MPH. The sample included 27 treatment-naive children with ADHD between the ages of 6 and 14. MPH administration started 1 day after the MRI acquisition. After a month, psychiatrists established the good or poor response to treatment according to clinical criteria. MRI images were analyzed using a technique based on regions of interest applied specifically to the caudate and accumbens nuclei. Sixteen patients showed good response to MPH and 11 a poor one. Regions of interest analysis showed that good responders had a higher concentration of gray matter in the head of both caudate nuclei and the right nucleus accumbens. Furthermore, a significant correlation was found between caudate and accumbens nuclei volume and the Conners’ Parent Rating Scale and Continuous Performance Test improvement. These results support the hypothesis of the involvement of the caudate and accumbens nuclei in MPH response and in ADHD pathophysiology.


Subthreshold disorders, conditions with relevant psychiatric symptoms which do not meet the full criteria of a disorder according to the prevailing classification systems, have received increased attention recently. The current paper aims to present a systematic review of subthreshold attention-deficit/hyperactivity disorder (ADHD) in children and adolescents. Searching five computerised databases (Ovid MEDLINE, PsycINFO, PubMed, Scopus, Web of Science) with two categories of search terms [(1) subclinical; subsyndromal; subthreshold (2) ADHD] the authors examined the prevalence of subthreshold ADHD among children and adolescents, the comorbidity of subthreshold ADHD and whether there was already any impact of subthreshold ADHD on functioning. Before these questions were answered, the included articles were examined to see what kinds of definitions of child and adolescent subthreshold ADHD are used and what kinds of assessments are used for measuring subthreshold ADHD among children and adolescents. The results of the 18 articles included show that different definitions of subthreshold ADHD in children and adolescents exist, a large variety of instruments are used, the prevalence rate of subthreshold ADHD is wide-ranging (0.8-23.1 %), the comorbidity of subthreshold ADHD is high and there are several
areas where subthreshold ADHD has a meaningful impact on functioning. All these suggest that focusing on subthreshold ADHD can be important in preventative interventions. The results of this systematic review support the dimensional approach of ADHD. Further research on uniform criteria of subthreshold ADHD is needed to support the inclusion of this condition in classification systems.

ALTERATIONS IN FAMILY STRUCTURE AND ADHD-RELATED SYMPTOMS AMONG THE AFFECTED CHILDREN.
Background: Attention-deficit/hyperactivity disorder (ADHD) is probably defined in a way that makes it the most common childhood psychiatric disorder worldwide with an estimated prevalence of 3-5%. The incidence of ADHD in many countries has been rising the last decades. ADHD has substantial impact on the affected children, their families, peers, and society. The disorder is characterized by pervasive symptoms of inattention, hyperactivity, and impulsivity. ADHD most often co-occurs with other psychiatric disorders. The etiology of ADHD is not well established, but both genetic and environmental factors like negative life events and stress in the social environment play a role. Parental divorce is a common and known stressor to the affected children; Alterations in family structure following the divorce has been associated with social adjustment problems in the affected children.
Objectives: We aimed to study if children in Denmark who had changed their family structure following a divorce show a higher level of ADHD-related symptoms compared to children living with both their parents.
Methods: Data on family structure and psychosocial symptoms were obtained from the 7-year follow up in The Danish National Birth Cohort. This cohort consists of about 100,000 Danish children born between 1996 and 2003. We used data from the parent-reported Strengths and Difficulties Questionnaire (SDQ), a standardized measure of emotional, behavioral, and social functioning in children and adolescents. We calculated mean with standard deviation of ADHD-related symptoms, differentiating according to whom the child lives with most of the time.
Results: Children living with one of their parents, one of their parents and a new partner, or equally with both parents had reports of more conduct problems, hyperactivity and peer problems than children living with both their parents. Children living with one parent and a new partner showed the highest level of conduct problems and hyperactivity compared to other family structure categories; the mean score of hyperactivity was 3.8 (SD=2.8) for children living with their father and his new partner, 3.2 (SD=2.5) for children living with their mother and her new partner, compared to 2.3 (SD 2.1) for children living with both their parents. The mean score of conduct problems showed a similar pattern.
Conclusions: In children who had divorced parents there were reported higher levels of ADHD-related symptoms compared with children living with both of their parents. This finding may be due to shared genetic factors in dysfunctional families or social stress exposure.

MATERNAL AGE AT CHILDBIRTH AND RISK FOR ADHD IN OFFSPRING.
Background: Women who give birth at younger ages (e.g., teenage mothers) are more likely to have children who exhibit behaviors problems, in particular antisocial behaviors. However, the link between early maternal age and offspring ADHD has not been established. In addition, it is not clear whether early maternal age at childbearing is causally associated with poor offspring outcomes or confounded by familial factors.
Method: The association between maternal age at childbirth and offspring's ADHD was studied using a large, nationally representative sample with quasi-experimental designs. We used children born in Sweden between 1992 and 1998 (N=720,764) and their mother identified from the Multi-generation Registry. Offspring ADHD (n=13,963) were identified from the National Patient Registry and the Prescribed Drug Registry. We also compared differentially exposed siblings to account for unmeasured familial factors that could account for the association. Further, children of siblings and children of twins comparisons were
conducted to identify the extent to which the association was confounded by genetic or environmental factors.

**Result:** Results showed that early maternal age at childbearing (maternal age <20) was significantly associated with the risk of ADHD in offspring (Hazard ratio =2.22, 95 % CI 2.06-2.38). Comparison of differentially exposed siblings indicated no within-family association. We further explored the association between maternal age at first birth (MAFB) and offspring ADHD using children of siblings and children of twins comparison, and the association was robust.

**Conclusion:** The results provided support for a causal association between MAFB and offspring ADHD, and the lack of within-family association could be explained by carry-over effect of MAFB on all siblings within a family.

Geographic Variation in the Prevalence of ADHD-GIS for a Better Understanding of the Aetiology of ADHD.

Laursen KB, Obel C, Simonsen M, et al.

**Background:** Attention Deficit Hyperactivity Disorder (ADHD) is probably the most common childhood psychiatric disorder with an estimated prevalence of 3-5 %. In Denmark as well as in several other countries the incidence of ADHD has been increasing for the last decades. However, little is known about the aetiology or the causes that could explain the rise in ADHD. Although studies suggest a strong heritability factor genetic factors cannot explain the epidemic occurrence and only changes in interaction with environmental risk factors can explain the rise in the incidence of the disorder. Other factors such as changes in the child up growth environment as well as more attention to the problem may be alternative explanations. The Geographic Information System (GIS) can be used to show the geographic variation in the occurrence of ADHD and by combining different indicators of ADHD including psychometrics, medication and diagnosis we expect to detect patterns that develop our understanding of this disorder.

**Objectives:** We aim to explore the use of GIS in detecting geographic patterns of ADHD distribution and relating those to different layers of information. We wish to examine the hypotheses that the diagnosis of ADHD will cluster in urban regions with easy access to diagnostic facilities whereas prescriptions of ADHD medication will vary more across the country showing a higher prevalence.

**Methods:** Our study population include all children born in Denmark between 1 January 1980 and 31 December 2005. We combine the use of register data from the Medical Birth Registry, the National Patient Registry on ICD-10 diagnosis of Hyperkinetic disorder (HKD), the National Prescription Database on ADHD medication and psychometric data from the National Birth Cohort and www.schoolhealth.eu.

**Results:** Preliminary results based on the ICD-10 diagnosis HKD alone suggested that there was a large geographic variation. There were 19,591 diagnosed with HKD of a total of 1,613,393 persons born in the period resulting in an overall prevalence of 12 per mille. However, the prevalence ranged from 0.4 to 40 per mille in towns of medium size in the eastern and northern part respectively. In the capital area the prevalence was higher in areas with lower social level. We will present a number of GIS maps to support the understanding of the geographical variation.

**Conclusions:** GIS mapping may be a promising tool in developing new causal models and may contribute to the development of specific hypotheses to be tested in other epidemiological designs.

Obesity and Physical Inactivity are Associated with ADHD Symptoms in Adolescents.

Khalife N, Kantomaa M, Glover V, et al.

**Background:** Recent evidence suggests that obesity and related factors, including physical inactivity, are co-morbid with attention deficit hyperactivity disorder (ADHD) symptoms. It is unknown whether specific subtype dimension(s) of ADHD contribute to the associations in the general population. We focus on the period of adolescence because it is a stage where adulthood health and lifestyle patterns are forming, and so is a key target for early intervention to prevent adverse health trajectories.
Objectives: By examining a large population-sample of adolescents (16 years) we aim to: Investigate bi-directional associations between obesity (body mass index [BMI] and waist-hip ratio [WHR]) and ADHD symptoms. Investigate the relative associations of specific ADHD symptom subtypes (inattention, hyperactivity-impulsivity and combined ADHD) with obesity/physical inactivity.

Methods: Data were obtained from the Northern Finland Birth Cohort (NFBC) 1986 (n=6856). Parents provided information on adolescent behaviour (using the Strengths and Weaknesses of ADHD symptoms and Normal behaviour [SWAN] scale), maternal education and family conditions. Data on BMI and WHR were obtained from clinical examinations. Adolescents self-reported their physical activity levels, which were then transformed to metabolic equivalent of task (MET) hours per week. We assessed the associations between obesity/physical inactivity (categorical) and ADHD symptoms (continuous) at 16 years using multiple regression analyses, controlling for gender, maternal education and change in family structure.

Results: We found significant bi-directional associations between obesity/physical inactivity and ADHD symptoms at 16 years. Obesity (BMI and WHR) predicted inattention symptoms (for BMI: $r=.03, p=.01$; for WHR: $r=.04, p=.01$); likewise, inattention symptoms predicted obesity (for BMI: OR 1.02, 95% CI 1.00-1.04; for WHR: OR 1.02, 95% CI 1.01-1.04). Physical inactivity predicted all ADHD symptoms (for combined ADHD symptoms: $r=.10, p<.001$; likewise all ADHD symptoms predicted physical inactivity (for combined ADHD symptoms: OR 1.01, 95% CI 1.01-1.02).

Conclusions: Our work supports the concept of co-morbidity between obesity/physical inactivity and ADHD symptoms in the general population of youth. Inattention symptoms in particular were associated with obesity, whilst all ADHD symptoms were linked with physical inactivity. This work highlights the importance of monitoring the eating patterns/behaviour and physical activity levels of youth with either ADHD or obesity, in order to enhance the diagnosis and treatment of both disorders. Ongoing work includes examining possible common genetic variations underlying obesity and ADHD, as well as longitudinal analyses, to investigate the directionality of these associations.


COMPARISON OF THE PHARMACOKINETICS AND CLINICAL EFFICACY OF NEW EXTENDED-RELEASE FORMULATIONS OF METHYLPHENIDATE.

Maldonado R.

INTRODUCTION: Attention-deficit hyperactivity disorder (ADHD) is a common neurobehavioral disorder of which the main features are inattention, hyperactivity and impulsivity. Methylphenidate (MPH) is the mainstay of treatment, but its short duration of action and consequent need for multiple administrations has been problematic for children attending school. Extended-release (ER) formulations have been developed to help overcome the drawbacks associated with immediate-release (IR) preparations.

AREAS COVERED: This review focuses on the pharmacokinetics of ER MPH formulations (Concerta(R), Equasym XL(R)/Metadata CD(R), Medikinet Retard(R) and Ritalin LA(R)). It also attempts to align the properties of each agent with available clinical findings in children/adolescents with ADHD.

EXPERT OPINION: In the author's opinion, Concerta, Equasym XL/Metadata CD, Medikinet Retard and Ritalin LA offer the convenience of once-daily administration with absorption characteristics resembling two or three times daily dosing with IR MPH preparations. All formulations produce plasma concentrations necessary to maintain symptom control during school time in children with ADHD. However, their pharmacokinetic profiles differ with respect to peak plasma levels and the rate at which peak levels are attained and decline. These differences may provide physicians with the opportunity to prescribe a formulation best suited to the symptom profile of individual patients. Additional clinical research is required to clarify further the relative merits of these ER formulations with the goal of enabling a more personalized approach to the management of children with ADHD.
OBJECTIVE: Attention-deficit/hyperactivity disorder (ADHD) is a psychiatric disorder affecting 5% of children. Methylphenidate (MPH) is a common medication for ADHD. Studies examining MPH's effect on pediatric ADHD patients' brain function using functional magnetic resonance imaging (fMRI) have not been compiled. The goals of this systematic review were to determine (1) which areas of the brain in pediatric ADHD patients are modulated by a single dose of MPH, (2) whether areas modulated by MPH differ by task type performed during fMRI data acquisition, and (3) whether changes in brain activation due to MPH relate to clinical improvements in ADHD-related symptoms.

METHODS: We searched the electronic databases PubMed and PsycINFO (1967-2011) using the following terms: ADHD AND (methylphenidate OR MPH OR ritalin) AND (neuroimaging OR MRI OR fMRI OR BOLD OR event related), and identified 200 abstracts, 9 of which were reviewed based on predefined criteria.

RESULTS: In ADHD patients the middle and inferior frontal gyri, basal ganglia, and cerebellum were most often affected by MPH. The middle and inferior frontal gyri were frequently affected by MPH during inhibitory control tasks. Correlation between brain regions and clinical improvement was not possible due to the lack of symptom improvement measures within the included studies.

CONCLUSIONS: Throughout nine task-based fMRI studies investigating MPH's effect on the brains of pediatric patients with ADHD, MPH resulted in increased activation within frontal lobes, basal ganglia, and cerebellum. In most cases, this increase "normalized" activation of at least some brain areas to that seen in typically developing children.

HNO. 2013 Jul;61:627-35.

PEDIATRIC ADHD: WHAT DOES THE OTOLARYNGOLOGIST NEED TO KNOW?
Gehrmann J, Brandl A

According to the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV) criteria, attention deficit hyperactivity disorder (ADHD) affects around 5% of all children and adolescents worldwide. The causes of ADHD are multifactorial, with a large genetic influence but also involvement of exogenic and psychosocial factors. Its core symptoms consist of attention deficits, hyperactivity and disruption of impulse control. It is important that symptoms appear before the age of six and are evident in multiple different situations, such as in familial and school environments. ADHD is a dimensional disorder, which means that the diagnostic process is time consuming, comprising a physical and neurological examination, behavioral observations and differentiated psychological assessments. In the field of otolaryngology, ADHD represents one of the important differential diagnoses to an auditory processing disorder (APD), alongside reading- and writing impairments and delayed speech development. In the instance of additional behavioral problems or more severe symptoms, it is advisable to transfer the patient to a specialized pediatrician or child and adolescent psychiatrist for appropriate counseling and treatment where required.


METHYLPHENIDATE-OSMOTIC-CONTROLLED RELEASE ORAL DELIVERY SYSTEM TREATMENT REDUCES PARENTING STRESS IN PARENTS OF CHILDREN AND ADOLESCENTS WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.

Objective: The aim of the current study was to investigate the effect of methylphenidate-osmotic release oral delivery system (MPH-OROS) treatment on parenting stress in parents of children and adolescents with attention-deficit/hyperactivity disorder (ADHD).

Methods: Four hundred and ninety-five children and adolescents (391 boys and 104 girls), aged 7 to 18 years who met the Diagnostic and Statistical Manual of Mental Disorders, fourth edition criteria for ADHD, were recruited at 48 psychiatric outpatient clinics across South Korea. Children's symptoms, parenting
stress, and parental depression were assessed at baseline, week 4, and week 8 of MPH-OROS treatment using the Korean version of the DuPaul's ADHD Rating Scale (ARS), the Beck's Depression Inventory (BDI), and the Parenting Stress Index, Short Form (PSI-SF).

**Results:** We found significantly decreased scores of ARS, parental BDI, and PSI-SF from baseline to week 4 and from week 4 to week 8. Also, there were positive correlations among baseline PSI-SF, ARS, and BDI scores. The changes in BDI and ARS scores were significantly associated with the PSI score changes, accounting for 20.1% and 10.0%, respectively.

**Conclusions:** We suggest that the increased parenting stress and depression in parents of children and adolescents with ADHD can be improved following the treatment with MPH-OROS.

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**ATTENTION DEFICIT HYPERACTIVITY DISORDER AND DUAL DISORDERS. EDUCATIONAL NEEDS FOR AN UNDERDIAGNOSED CONDITION.**

Martinez-Raga J, Szerman N, Knecht C, et al.

A wide range of comorbid psychiatric disorders overlap with attention-deficit hyperactivity disorder (ADHD) across the life span. There is a robust and complex link between ADHD and substance use disorders (SUD). The aim of this report was to review the neurobiological and other vulnerability factors explaining the comorbidity of ADHD and an addictive disorder, as well as the key aspects of the assessment and diagnosis of dually diagnosed ADHD patients. A comprehensive and systematic search of relevant databases (PubMed, Embase, and PsychINFO) was conducted to identify studies published in peer-reviewed journals until July 31, 2012, with the aim of exploring the association of ADHD and SUD with postgraduate training and residency education. Across the life span, ADHD is associated with significant impairment and comorbidity. Data from epidemiological, clinical and epidemiological studies show a very solid link between ADHD and SUD. Therefore, it is very important to carefully and systematically assess for any substance use in patients with suspected ADHD coming to initial assessment, and vice versa. While there are various valid and reliable rating and screening scales, diagnosis cannot solely rely on any of the instruments available for both SUD and ADHD in adult patients with dual pathology. The most important and effective tool in the assessment of dually diagnosed patients with ADHD and SUD is a full and comprehensive clinical and psychosocial assessment. Hence, it is essential to actively incorporate training opportunities on the assessment, diagnosis, and management of adult ADHD and dually diagnosed ADHD patients during postgraduate education residency or specialist training.

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**GESTATIONAL OVERGROWTH AND UNDERGROWTH AFFECT NEURODEVELOPMENT: SIMILARITIES AND DIFFERENCES FROM BEHAVIOR TO EPIGENETICS.**

Grissom NM, Reyes TM.

The size of an infant at birth, a measure of gestational growth, has been recognized for many years as a biomarker of future risk of morbidity. Both being born small for gestational age (SGA) and being born large for gestational age (LGA), are associated with increased rates of obesity and metabolic disorder, as well as a number of mental disorders including attention deficit/hyperactivity disorder, autism, anxiety, and depression. The common risks raise the question of what neurobiological mechanisms are altered in SGA and LGA offspring. Here we review recent findings allowing for direct comparison of neurobiological outcomes of SGA and LGA in human and animal models. We also present new data highlighting similarities and differences in behavior and neurobiology in our mouse models of SGA and LGA. Overall, there is significant data to support aberrant epigenetic mechanisms, particularly related to DNA methylation, in the brains of SGA and LGA offspring, leading to disruptions in the cell cycle in development and gene expression in adulthood.
REVIEW OF CURRENT EVIDENCE ON THE IMPACT OF PESTICIDES, POLYCHLORINATED BIPHENYLS AND SELECTED METALS ON ATTENTION DEFICIT / HYPERACTIVITY DISORDER IN CHILDREN.

Polanska K, Jurewicz J, Hanke W.

The aim of this review was to investigate the association between attention deficit / hyperactivity disorder (ADHD) or ADHD-related symptoms and industrial chemicals, such as organophosphates and organochlorine pesticides, polychlorinated biphenyls (PCBs), lead, mercury and manganese. Medline, PubMed and EBSCO searches were performed to identify the studies that analyzed the association of prenatal and postnatal child exposure to such toxicants and ADHD or ADHD-related symptoms. The review is restricted to human studies published in English in peer-reviewed journals since 2000. Most of the presented studies focused on pesticides, PCB and lead. The impact of mercury and manganese was investigated less frequently. The findings indicate that children's exposure to organophosphate pesticides may cause symptoms consistent with pervasive developmental disorder, ADHD or attention problems. Exposures to organochlorine pesticides and PCBs were associated with ADHD-like behaviors such as alertness, quality of alert response, and cost of attention. The studies provided evidence that blood lead level below 10 μg/dl was associated with ADHD or ADHD-related symptoms. Information on the association between exposure to mercury and neurotoxicity is limited, and requires further confirmation in future research. Two studies indicated that exposure to manganese is related to ADHD; such exposure and its impact on children neurodevelopment need to be further investigated. Future studies should use a prospective design with multiple biological samples collected over time for better assessment of exposure and its critical windows. Additionally, inclusion of potential confounding factors and co-exposures is crucial.

METHYLPHENIDATE TREATMENT IN CHILDREN WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER AND COMORBID SOCIAL PHOBIA.

Golubchik P, Sever J, Weizman A.

The aim of this study was to assess the response of social phobia (SP) symptoms to methylphenidate (MPH) treatment in children with attention deficit hyperactivity disorder (ADHD). Twenty-one ADHD patients with SP, aged between 8 and 18 years, received 12 weeks of MPH treatment. The severity of SP symptoms were assessed by the Liebowitz Social Anxiety Scale for Children and Adolescents (LSAS-CA), and the severity of ADHD symptoms was assessed by the ADHD Rating Scale at baseline and at endpoint. MPH treatment was associated with a significant decrease in the ADHD Rating Scale scores (P<0.0001) and in the total LSAS-CA scores (P=0.013), as well as the school-related items of LSAS-CA (P=0.011). A significant correlation was found between the reductions in ADHD score and total LSAS-CA score (P=0.038), especially in school-related SP. The improvement in ADHD symptoms because of MPH treatment correlates with a parallel improvement in SP. MPH treatment appears to be safe and effective in ADHD/SP children.

SELF-INSERTED FOREIGN BODY AND ATTENTION-DEFICIT/HYPERACTIVITY DISORDER: EVALUATED BY THE CONNERS’ PARENT RATING SCALES-REVISED.

Ozcan K, Ozcan T, Muluk NB, et al.

Objectives: We aimed to evaluate the relationship between attention-deficit/hyperactivity disorder (ADHD) and self-inserted foreign bodies (SIFBs) in children by the Conners’ Parent Rating Scales-Revised (CPRS-R).

Methods: Forty-five children (31 males and 14 females) with self-inserted foreign body of ear/nose and 37 healthy children (22 males and 15 females) included into the study. They were all between 3 and 9 years old. The parents filled the socio-demographic information form including age, gender, demographic data, previous medical history of the child and features of the family; and completed the Conners’ Parent Rating Scales-Revised (CPRS-R) questionnaire.
**Results:** In the SIFB group (study), 55.6% of the children were not attending to the school, 31.1% of them were attending to the primary school and 13.3% of them were the pre-school student. These rates were 37.8%, 32.4% and 29.7%, respectively, in the control group. The all CPRS-R subscale values (CG/I, H, ADHD-I, CGI-DI, DSMIV SS-I, DSM-IV SS-HI and DSM-IV SS-T) were significantly higher in the study group than the control group. There was no significant correlation between gender of the children and CPRS-R subscales. Children with lower school success, and having previous psychiatric problems were related to higher CPRS-R values in all subscales. In older children, hyperactivity scores were lower; and in younger children and the children, not going to the school, hyperactivity scores were higher. CPRS-R scores decreased as the child grown.

**Conclusion:** It was concluded that children with ADHD were more likely to have conditions that might damage himself/herself such as self-inserted foreign body or trauma than normal children. To avoid this condition, these families should closely observe the child; and the child should be provided to participate in activities such as group games and activities that contribute to the development of the child. Warning the children properly and close follow-up of the young children are required to prevent this unwanted condition.

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**Cognitive Functioning and Physical Health in Older Adults with ADHD Aged 61-94 Years.**

**Semeijn E, Korten N, Comijs H, et al.**

**Objectives:** An emerging body of research shows cognitive deficits in children and younger adults with Attention-Deficit/Hyperactivity Disorder (ADHD). To our knowledge no studies have focused on cognitive functioning in older adults with ADHD. Therefore the present study investigates the association between ADHD and cognitive functioning in older adults.

**Method:** Data were collected in a twophase sampling side-study (2008-2009) in the Longitudinal Aging Study Amsterdam. Data on ADHD symptoms and cognitive functioning was collected from two hundred twenty three randomly selected LASA respondents aged 61 to 94 years during home visits. ADHD symptoms and ADHD diagnosis were assessed with the DIVA 2.0. Cognitive functioning was assessed with tests in the domains of executive functioning, information processing speed, memory, and attention/working memory.

**Results:** Regression analyses show that ADHD diagnosis (B=-0.45, p=0.02) and ADHD severity (B=-0.02, p=0.04) were negatively associated with cognitive functioning in the attention/working memory domain, but not with other cognitive domains. When adjusting for depression these associations were no longer significant (B=-0.32, p=0.11 respectively B=-0.01, p=0.25).

**Conclusion:** The study shows that ADHD in older adults is associated with poorer cognitive functioning in the attention/working memory domain. However, this association was partly explained by depressive symptoms.

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**Personality Characteristics and Comorbid Anxiety and Depression Symptoms Among Older Adults with ADHD.**

**Michielsen M, Comijs H, Semeijn E, et al.**

**Objective:** Both comorbidity between ADHD and depression and anxiety and the relationship between ADHD and personality characteristics such as low self-esteem and Neuroticism have been well documented in children and young to middleaged adults with ADHD. Yet, little is known about these relationships in older adults with ADHD. In this presentation two studies will be discussed. The first study examined the comorbidity of anxiety and depressive symptoms among older adults with ADHD. This was examined both using cross-sectional and longitudinal data. The other study examined the association between ADHD and personality characteristics and the possible mediating role of personality characteristics between ADHD and depressive symptoms in older adults.

**Method:** Data were used from the Longitudinal Aging Study Amsterdam (LASA). In the first study participants were examined in three measurement cycles, covering six years. They were asked about...
depressive and anxiety symptoms. In the second study personality characteristics were examined cross-sectionally. To diagnose ADHD, the DIVA 2.0, a diagnostic interview was administered among a subsample (N=231, age 60-94). Data were analyzed by means of linear regression analyses and linear mixed models.

Results: Study 1: ADHD diagnosis was associated with more anxiety and depressive symptoms, crosssectionally as well as longitudinally. Study 2: preliminary results show that older adults with ADHD have low self-esteem, low self-efficacy, low sense of mastery and high levels of Neuroticism and Social Inadequacy. The relationship between ADHD and depressive symptoms seems to be partly mediated by mastery, Neuroticism and Social Inadequacy.

Conclusion: It appears that the association between ADHD and anxiety/depression remains in place with aging. In addition, the relationship between ADHD and depression is partly mediated by mastery, Neuroticism and Social Inadequacy. This suggests that, in clinical practice, directing attention to ADHD, personality characteristics and comorbid disorders may be fruitful.


THE RELATIONSHIPS BETWEEN ATTENTION DEFICIT HYPERACTIVITY DISORDER AND SOCIAL FUNCTIONING AND PARTICIPATION IN OLDER ADULTS IN A POPULATION-BASED STUDY.
Michielsen M, Semeijn E, Comijs H, et al.

Objective: Attention-deficit/hyperactivity disorder in children and adults have shown a negative influence on social functioning and social participation (e.g., work participation). Yet, in older adults little is known about these associations. Therefore the aim of this study is to examine the associations between ADHD and social functioning and participation among older adults.

Method: Data were used from the Longitudinal Aging Study Amsterdam (LASA). In 2008/2009 respondents were asked about social functioning and participation. A diagnostic interview to diagnose ADHD was administered among a subsample (N=231, age 60-94). ADHD was measured by means of ADHD diagnosis and level of ADHD symptoms. Data were analyzed by means of linear, logistic and multinomial logistic regression analyses.

Results: ADHD diagnosis was associated with being divorced/never married (OR=3.39, p=0.03), having less family members in their network (B=-0.40, p=0.01) and emotional loneliness (B=0.97, p=0.02). Level of ADHD symptoms was associated with more emotional support given (B=0.01, p = 0.05), emotional (B=0.04, p=0.04) and social loneliness (B=0.03, p=0.03), greater recreational social participation (B=0.04, p=0.01) and with lower income level (OR=1.05, P=0.05). Depressive symptoms play an important role in the association between ADHD and loneliness.

Conclusion: This study is the first epidemiological study examining the association between ADHD and social functioning and social participation among older adults. This study shows that ADHD in old age is related to being divorced/never married and loneliness but not to work participation. Psychogeriatric practices should direct their attention to loneliness when treating ADHD.


EVIDENCE FOR A MULTI-DIMENSIONAL LATENT STRUCTURAL MODEL OF EXTERNALIZING DISORDERS.
Witkiewitz K, King K, McMahon RJ, et al.

Strong associations between conduct disorder (CD), antisocial personality disorder (ASPD) and substance use disorders (SUD) seem to reflect a general vulnerability to externalizing behaviors. Recent studies have characterized this vulnerability on a continuous scale, rather than as distinct categories, suggesting that the revision of the Diagnostic and Statistical Manual of Mental Disorders (DSM-5) take into account the underlying continuum of externalizing behaviors. However, most of this research has not included measures of disorders that appear in childhood [e.g., attention-deficit/hyperactivity disorder (ADHD) or oppositional defiant disorder (ODD)], nor has it considered the full range of possibilities for the latent structure of externalizing behaviors, particularly factor mixture models, which allow for a latent factor to have both continuous and categorical dimensions. Finally, the majority of prior studies have not tested
multidimensional models. Using lifetime diagnoses of externalizing disorders from participants in the Fast Track Project (n=715), we analyzed a series of latent variable models ranging from fully continuous factor models to fully categorical mixture models. Continuous models provided the best fit to the observed data and also suggested that a two-factor model of externalizing behavior, defined as (1) ODD+ADHD+CD and (2) SUD with adult antisocial behavior sharing common variance with both factors, was necessary to explain the covariation in externalizing disorders. The two-factor model of externalizing behavior was then replicated using a nationally representative sample drawn from the National Comorbidity Survey-Replication data (n=5,692). These results have important implications for the conceptualization of externalizing disorders in DSM-5.


**BIDIRECTIONAL RELATIONS BETWEEN PARENTING PRACTICES AND CHILD EXTERNALIZING BEHAVIOR: A CROSS-LAGGED PANEL ANALYSIS IN THE CONTEXT OF A PSYCHOSOCIAL TREATMENT AND 3-YEAR FOLLOW-UP.**


In the current study, we examined longitudinal changes in, and bidirectional effects between, parenting practices and child behavior problems in the context of a psychosocial treatment and 3-year follow-up period. The sample comprised 139 parent-child dyads (child ages 6-11) who participated in a modular treatment protocol for early-onset ODD or CD. Parenting practices and child behavior problems were assessed at six time-points using multiple measures and multiple reporters. The data were analyzed using cross-lagged panel analyses. Results indicated robust temporal stabilities of parenting practices and child behavior problems, in the context of treatment-related improvements, but bidirectional effects between parenting practices and child behavior were less frequently detected. Our findings suggest that bidirectional effects are relatively smaller than the temporal stability of each construct for school-age children with ODD/CD and their parents, following a multi-modal clinical intervention that is directed at both parents and children. Implications for treatment and intervention are discussed.


**WORKING MEMORY DEFICITS IN ADULTS WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER (ADHD): AN EXAMINATION OF CENTRAL EXECUTIVE AND STORAGE/REHEARSAL PROCESSES.**


The current study was the first to use a regression approach to examine the unique contributions of central executive (CE) and storage/rehearsal processes to working memory (WM) deficits in adults with ADHD. Thirty-seven adults (ADHD=21, HC=16) completed phonological (PH) and visuospatial (VS) working memory tasks. While both groups performed significantly better during the PH task relative to the VS task, adults with ADHD exhibited significant deficits across both working memory modalities. Further, the ADHD group recalled disproportionately fewer PH and VS stimuli as set-size demands increased. Overall, the CE and PH storage/rehearsal processes of adults with ADHD were both significantly impaired relative to those of the healthy control adults; however, the magnitude of the CE effect size was much smaller compared to previous studies of children with the disorder. Collectively, results provide support for a lifelong trajectory of WM deficits in ADHD.

J Affect Disord. 2013 May;147:164-70.

**PERSONAL AND FAMILIAL CORRELATES OF BIPOLAR (BP)-I DISORDER IN CHILDREN WITH A DIAGNOSIS OF BP-I DISORDER WITH A POSITIVE CHILD BEHAVIOR CHECKLIST (CBCL)-SEVERE DYSREGULATION PROFILE: A CONTROLLED STUDY.**


**BACKGROUND:** Although the DSM-IV provides explicit criteria for the diagnosis of BP-I disorder, this is a complex diagnosis that requires high levels of clinical expertise. Previous work shows children with a
unique profile of the CBCL of high scores (2SD) on the attention problems (AP), aggressive behavior (AGG), and anxious-depressed (AD) (A-A-A) subscales are more likely than other children to meet criteria for BP-I disorder in both epidemiological and clinical samples. However, since not all BP-I disorder children have a positive profile questions remain as to its informativeness, particularly in the absence of an expert diagnostician.

METHODS: Analyses were conducted comparing personal and familial correlates of BP-I disorder in 140 youth with a structured interview and an expert clinician based DSM-IV diagnosis of BP-I disorder with (N=80) and without (N=60) a positive.


AGE DIFFERENCES IN THE PHENOMENOLOGY OF PEDIATRIC BIPOLAR DISORDER.
Demeter CA, Youngstrom EA, Carlson GA, et al.

BACKGROUND: The primary purpose of this study was to explore whether age differences in the phenomenology of bipolar disorders from 4 to 17 years of age exist.

METHODS: Outcome measures included questionnaires pertaining to mood symptoms, psychosocial functioning, and family history of psychiatric illness. Phenomenology was examined in two diagnostic groups: syndromal bipolar disorder (bipolar I or II) and subsyndromal bipolar disorder (bipolar disorder not otherwise specified or cyclothymia) and across six age cohorts: 4-6, 7-8, 9-10, 11-13, and 14-17 years. Analyses examined linear and non-linear age effects on clinician-rated measures of mood and psychosocial functioning.

RESULTS: Participants were 535 outpatients (339 males) ages 4-17 years. The proportion diagnosed with comorbid ADHD was significantly lower in the oldest age group. Age groups showed significant moderate decreases in motor activity, aggression, and irritability with age. Many symptoms of depression showed significant increases with age. BP I cases showed much higher manic symptoms, and BP I and BP II cases indicated slightly to moderately higher depressive symptoms, compared to subsyndromal cases. These patterns held after adjusting for comorbid ADHD, and age did not interact with syndrome status. There were also age differences in total scores for measures of mood symptoms and psychosocial functioning.

LIMITATIONS: Mood ratings were completed based on the same interview that informed the research diagnoses. Also, mood episode at time of interview was not captured.

CONCLUSIONS: These findings affirm the existence of bipolar disorder from pre-school children through adolescence, with a similar clinical presentation across a wide developmental age span.


PRE-TRIAL REPORTED DEFENDANTS IN THE NETHERLANDS WITH INTELLECTUAL DISABILITY, BORDERLINE AND NORMAL INTELLECTUAL FUNCTIONING.
Vinkers DJ.

BACKGROUND: Intellectually disabled offenders may have different characteristics than offenders with average intellectual functioning. We therefore compared pre-trial reported defendants with an IQ score \( \leq 70, 71-84 \) and \( \geq 85 \) points.

METHODS: Nationwide database of pre-trial psychiatric reports requested by Dutch courts between 2000 and 2006 with a reported level of intellectual functioning (n=12 186).

RESULTS: Defendants with an IQ score between 71 and 84 (n=2 439 reports; 20.0%) and \( \leq 70 \) (n=539 reports; 4.4%) were younger, more often from an ethnic minority and more often diagnosed with psycho-organic syndromes, developmental and conduct disorders as compared with defendants with an IQ score of 85 or higher. In addition, there was an increased risk of attention deficit hyperactivity disorder and rape as indicted crime and a decreased odds ratio of having a steady job and cannabis abuse in defendants with an IQ score of 71-84.
CONCLUSION: Intellectually disabled defendants have different characteristics than defendants without intellectually disability.


ADOLESCENT OUTCOME OF CHILD ADHD IN PRIMARY CARE SETTING: STABILITY OF DIAGNOSIS.
Srebnicki T, Kolakowski A, Wolanczyk T.

OBJECTIVE: The aim of the study was to assess the functioning of patients with ADHD 6 to 7 years after the diagnosis. One objective was to determine the stability of diagnosis, symptoms decline, subtype change, remission, and change of diagnosis.

METHOD: In all, 101 participants were chosen for testing. All were interviewed for the presence of ADHD and social, academic, and peer functioning, and completed Youth Self-Report. The caregivers completed a Wender Utah Rating Scale and Child Behavior Checklist, and were asked to assess the social, academic, and peer functioning of their offspring.

RESULTS: A total of 56% (n=57) still met the criteria for ADHD and 24.7% (n=25) still met the criteria for hyperkinetic disorder (HKD). Subtype migration was observed. In all, 7.7% (n=14) were rediagnosed with Asperger's syndrome, 2.2% (n=4) received a diagnosis of bipolar disorder, 2.2% (n=4) were diagnosed with mental retardation, 1 with schizophrenia, and 1 with genetic disorder.

CONCLUSION: The reliability of diagnosis was high. The rates of all subtypes of ADHD decreased. More measures need to be taken in terms of differential diagnosis of ADHD and Asperger's Syndrome.


PREDICTION OF ADHD TO ANXIETY DISORDERS: AN 11-YEAR NATIONAL INSURANCE DATA ANALYSIS IN TAIWAN.
Tai YM, Gau CS, Gau SS, et al.

OBJECTIVE: To prospectively investigate prediction of ADHD to anxiety disorders (ANXs) in a national sample of Taiwan.

METHOD: From the Taiwan National Health Insurance Dataset (1997-2007), we collected 2,385 cases of new diagnoses of ADHD from 1999 to 2003 and 9,540 sex-, age- and index dates of the first diagnosis of ADHD-matched cohort controls without ADHD. The outcome is age of the first diagnosis of ANXs until December 31, 2007.

RESULTS: More cases of ADHD (17.7%) developed ANXs than did matched controls (1.9%) with a younger age onset (12.7 years vs. 17.9 years) and a shorter "survival time" (1.4 years vs. 5.0 years). Cox models revealed a significant prediction of ADHD to ANXs controlling for other psychiatric comorbidities [Hazard ratio (HR) =15.83]. The magnitude of such association was greater in males and decreased with older age of first ADHD diagnosis.

CONCLUSION: The findings imply that early detection and treatment for ADHD may offset later development of ANXs.


PRE- AND POSTNATAL RISK FACTORS FOR ADHD IN A NONCLINICAL PEDIATRIC POPULATION.
Sagiv SK, Epstein JN, Bellinger DC, et al.

OBJECTIVE: The authors characterized pre- and postnatal risk factors for ADHD among a population-based sample of 8-year-old children followed since birth (N=604).

METHOD: Parents and teachers rated ADHD symptoms, including inattention and impulsivity/hyperactivity. The authors reviewed pediatric medical records for history of an ADHD diagnosis, and parents reported ADHD medication use. The authors analyzed risk factors in relationship to outcomes using multivariable regression models.

RESULTS: Low paternal education, prenatal smoking, prenatal illicit drug use, maternal depression, and low Home Observation for Measurement of the Environment score were associated with greater risk for
ADHD behaviors assessed via rating scale. Low income and being male were associated with ADHD diagnosis in medical records and ADHD medication use.

**CONCLUSION:** The authors found associations between socioeconomic, psychosocial, and prenatal exposures and ADHD-related behavior. Selection bias due to access to care and recall bias from inaccurate report of past exposures is minimized in this large, nonclinical, prospective cohort study.


**ADHD MEDICATION VACATIONS AND PARENT-CHILD INTERACTIONS BY GENDER.**

*Barnard-Brak L, Schmidt M, Sulak T.*

**OBJECTIVE:** The purpose of the current study was to examine medication vacations among children with ADHD according to parent-child dyads (e.g., mother-son, father-daughter, mother-daughter, and father-son).

**METHOD:** In a survey study of 259 parents of children with ADHD, the use of medication vacations according to parent-child sex dyads was examined.

**RESULTS:** Results of the current study suggest that fathers seem to report endorsing medication vacations more with their sons with ADHD as opposed to their daughters with ADHD. There did not seem to be any significant differences among mothers.

**CONCLUSION:** Results of the current study conclude with directions for future research and practice.


**DO SYMPTOMS OF SLUGGISH COGNITIVE TEMPO IN CHILDREN WITH ADHD SYMPTOMS REPRESENT COMORBID INTERNALIZING DIFFICULTIES?**


**OBJECTIVE:** Symptoms of sluggish cognitive tempo (SCT) are correlated with inattention and internalizing difficulties. The purpose of the present study was to determine whether symptoms of SCT reflect comorbid internalizing disorder with ADHD or a separate syndrome.

**METHOD:** Using a clinical sample of youth evaluated for behavioral and learning difficulties (N=73), this study examined whether SCT remains associated with symptoms of ADHD after accounting for comorbid symptoms of anxiety and depression reported by children and parents.

**RESULTS:** SCT symptoms were correlated with inattention and parent reports of child depression, but not with parent-reported anxiety or child reports of internalizing problems. Inattention (in the absence of hyperactivity/impulsivity) remained uniquely associated with SCT even after accounting for internalizing problems.

**CONCLUSION:** The findings confirm SCT as a correlate of inattention and support its construct validity as separate from comorbid internalizing problems. Further research on the clinical utility of SCT is needed.


**A NEUROPSYCHOLOGICAL PERSPECTIVE ON ATTENTION PROBLEMS IN NEUROFIBROMATOSIS TYPE 1.**

*Templer AK, Titus JB, Gutmann DH.*

Cognitive problems are common in children with neurofibromatosis type 1 and they can often complicate treatment. The current literature review examines cognitive functioning in neurofibromatosis type 1, with a specific focus on executive functioning. This includes exploration of how deficits in executive functioning are expressed in children with neurofibromatosis type 1 and how these deficits contrast with ADHD. The value of investigating subcomponents of executive functioning is discussed, as are implications for effective treatment and future research.
BRAIN CORTICAL THICKNESS IN ADHD: AGE, SEX, AND CLINICAL CORRELATIONS. 

OBJECTIVE: Longitudinal magnetic resonance imaging (MRI) studies have shown reduced cortical thickness (CT) in individuals with ADHD, but this abnormality disappears with age, suggesting developmental delay. However, cross-sectional MRI studies have shown reduced CT, suggesting abnormal development. The aim of this study was to compare whole-brain CT in male and female children, adolescents, and adults with ADHD with whole-brain CT in matched control participants.

METHOD: MRI scans were performed on ADHD and control participants.

RESULTS: CT data revealed differences in right hemisphere (RH) only. Reduced CT was observed predominantly in the frontoparietal region. However, increased CT was observed predominantly in the occipital lobe. The CT differences were correlated with severity of ADHD. Analysis of sex differences revealed that location, number, and magnitude of CT differences were different between males and females in each age group.

CONCLUSION: These data support the hypothesis that anatomical abnormalities in ADHD represent abnormal development rather than developmental delay.

TRAINING EXECUTIVE, ATTENTION, AND MOTOR SKILLS: A PROOF-OF-CONCEPT STUDY IN PRESCHOOL CHILDREN WITH ADHD.
Halperin JM, Marks DJ, Bedard AC, et al.

OBJECTIVE: To examine whether cognitive enhancement can be delivered through play to preschoolers with ADHD and whether it would affect severity of ADHD symptoms.

METHOD: Twenty-nine 4- and 5-year-old children and their parents participated in separate group sessions (3-5 children/group). Child groups were introduced games designed to enhance inhibitory control, working memory, attention, visuospatial abilities, planning, and motor skills. Parent groups were encouraged playing these games with their children at least 30 to 45 min/day and taught strategies for scaffolding difficulty levels and dealing with obstacles to daily playing.

RESULTS: Parent ratings and session attendance indicated considerable satisfaction with the program. Parent (p < .001) and teacher (p = .003) ratings on the ADHD-Rating Scale-IV (ADHD-RS-IV) indicated significant improvement in ADHD severity from pre- to post-treatment, which persisted 3 months later.

CONCLUSION: This play-based intervention for preschoolers with ADHD is readily implemented at home. Preliminary evidence suggests efficacy beyond the termination of active treatment.

EFFICACY OF ATOMOXETINE FOR THE TREATMENT OF ADHD SYMPTOMS IN PATIENTS WITH PERSISTENT DEVELOPMENTAL DISORDERS: A PROSPECTIVE, OPEN-LABEL STUDY. 

OBJECTIVE: Atomoxetine’s tolerance and efficacy were studied in 24 patients with pervasive developmental disorder and symptoms of ADHD.

METHOD: Prospective, open-label, 16-week study was performed, using the variables of the Clinical Global Impression Scale and the Conners’ Scale, among others.

RESULTS: A significant difference was found between pre- and posttreatment scores as well as a significant reduction was found on the scales used. Only five patients presented adverse events.

CONCLUSION: Atomoxetine therefore appears to be a useful drug, pointing to the need for larger, randomized, controlled, double-blind studies to confirm its efficacy versus placebo and in comparison with other treatment options.
THE DIRECT EFFECTS OF INATTENTION AND HYPERACTIVITY/IMPULSIVITY ON PEER PROBLEMS AND MEDIATING ROLES OF PROSOCIAL AND CONDUCT PROBLEM BEHAVIORS IN A COMMUNITY SAMPLE OF CHILDREN.

Andrade BF, Tannock R.

OBJECTIVE: This study tested whether children's symptoms of inattention and hyperactivity/impulsivity were associated with peer problems and whether these associations were mediated by conduct problems and prosocial behaviors.

METHOD: A community sample of 500 children, including 245 boys and 255 girls, who ranged in age from 6 to 9 years (M=7.6, SD=0.91) were recruited. Teachers' report of children's inattention, hyperactivity/impulsivity, conduct problems, prosocial behaviors, and peer problems was collected.

RESULTS: Symptoms of inattention and hyperactivity/impulsivity were significantly positively associated with peer problems. Conduct problems were associated with more peer problems and prosocial behaviors with less peer problems. Conduct problems and prosocial behaviors partially mediated the association between hyperactivity/impulsivity and peer problems and fully mediated the inattention-peer problems association.

CONCLUSION: Findings show that prosocial behaviors and conduct problems are important variables that account for some of the negative impact of symptoms of inattention and hyperactivity/impulsivity on peer functioning.

COMPARISON OF MOTHER, FATHER, AND TEACHER REPORTS OF ADHD CORE SYMPTOMS IN A SAMPLE OF CHILD PSYCHIATRIC OUTPATIENTS.

Sollie H, Larsson B, Morch WT.

OBJECTIVE: To explore the significance of adding father ratings to mother and teacher ratings in the assessment of ADHD symptoms in children.

METHOD: The ADHD Rating Scale-IV, the Child Behavior Checklist, and the Teacher Report Form were filled out by all three informants for a sample of 48 clinically referred children (79% boys) aged 6 to 15 (M=10.1) years.

RESULTS: Correspondence between father and teacher reports on ADHD-specific symptoms (intraclass correlation coefficient [ICC] =.38) exceeded that between mothers and teachers (ICC=.23). Fathers rated their children as having fewer problems than did mothers and teachers on Total scale scores and the Inattention subscale of the ADHD Rating Scale-IV. Mother ratings were more sensitive to an ADHD diagnosis, whereas father ratings better predicted an ADHD diagnosis requiring the two-setting criterion.

CONCLUSION: The choice of parent informant and informant combination had a considerable impact on parent-teacher concordance and estimates of ADHD symptoms and subtypes in the child.

SLUGGISH COGNITIVE TEMPO AMONG YOUNG ADOLESCENTS WITH ADHD: RELATIONS TO MENTAL HEALTH, ACADEMIC, AND SOCIAL FUNCTIONING.

Becker SP, Langberg JM.

OBJECTIVE: This study investigated the role of sluggish cognitive tempo (SCT) in relation to externalizing and internalizing mental health problems, academic functioning, and social functioning among young adolescents with attention-deficit/hyperactivity disorder (ADHD).

METHOD: In all, 57 youth ages 10 to 14 participated in the study. Parents rated SCT, internalizing, and externalizing symptoms, as well as social and academic impairment. Teachers rated academic and peer impairment, and intelligence and academic achievement also were assessed.

RESULTS: Above and beyond ADHD and conduct problem symptoms, SCT was associated with internalizing mental health symptoms and social problems. The association between SCT and externalizing problems or academic functioning was not significant when accounting for ADHD symptomatology and intelligence.
CONCLUSION: SCT is consistently associated with internalizing symptoms and is also associated with young adolescents' general social difficulties. When controlling for important related constructs, SCT is not associated with externalizing symptoms or academic impairment among young adolescents with ADHD.


ATOMOXETINE FOR TREATING ADHD SYMPTOMS IN AUTISM: A SYSTEMATIC REVIEW.
Ghanizadeh A.

OBJECTIVE: This study systematically reviews the current literature on the administration of atomoxetine for treating children and adolescents with comorbidity on autism spectrum disorder (ASD) and ADHD.
METHOD: PubMed/Medline and Google Scholar databases were electronically searched to find the published trials on atomoxetine and ASD.
RESULTS: Six articles reported the clinical trials of atomoxetine for treatment of ADHD symptoms in patients with autism or pervasive development disorders. Only one study that was placebo-controlled crossover pilot trial reported that it is effective. Atomoxetine may be effective in high-functioning patients with autism or patients with low severity. Those with high severity of ASD may be more vulnerable to the adverse effects of atomoxetine.
CONCLUSION: There are not enough controlled clinical trials for showing the efficacy of atomoxetine for treatment of ADHD symptoms in autism. Although evidence suggests potential efficacy of atomoxetine, the current evidences are not conclusive.


A NOVEL GROUP THERAPY FOR CHILDREN WITH ADHD AND SEVERE MOOD DYSREGULATION.

OBJECTIVE: No psychosocial treatments have been developed for children with ADHD and severe mood dysregulation (SMD) despite the significant prevalence and morbidity of this combination. Therefore, the authors developed a novel treatment program for children with ADHD and SMD.
METHOD: The novel therapy program integrates components of cognitive-behavioral therapies for affect regulation with a parent-training intervention for managing recurrent defiant behaviors. It consists of nine 105-min child and parent groups run in unison. A pilot trial was conducted with seven participants with ADHD and SMD ages 7 to 12 who were on a stable stimulant regimen.
RESULTS: Six of the seven (86%) families completed the program. Participants showed large improvements in depressive symptoms, mood lability, and global functioning. Milder improvements in externalizing behaviors were observed.
CONCLUSION: Results suggest the feasibility and potential efficacy of the therapy program for children with ADHD and SMD and warrant a larger controlled trial.

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FROM THE EDITOR-IN-CHIEF’S DESK.
Kopelwicz HS.

THE EFFECT OF EARLY DEPRIVATION ON EXECUTIVE ATTENTION IN MIDDLE CHILDHOOD.
BACKGROUND: Children reared in deprived environments, such as institutions for the care of orphaned or abandoned children, are at increased risk for attention and behavior regulation difficulties. This study examined the neurobehavioral correlates of executive attention in post institutionalized (PI) children.
METHODS: The performance and event-related potentials (ERPs) of 10- and 11-year-old internationally adopted PI children on two executive attention tasks, go/no-go and Flanker, were compared with two groups: children internationally adopted early from foster care (PF) and nonadopted children (NA).

RESULTS: Behavioral measures suggested problems with sustained attention, with PIs performing more poorly on go trials and not on no-go trials of the go/no-go and made more errors on both congruent and incongruent trials on the Flanker. ERPs suggested differences in inhibitory control and error monitoring, as PIs had smaller N2 amplitude on go/no-go and smaller error-related negativity on Flanker.

CONCLUSIONS: This pattern of results raises questions regarding the nature of attention difficulties for PI children. The behavioral errors are not specific to executive attention and instead likely reflect difficulties in overall sustained attention. The ERP results are consistent with neural activity related to deficits in inhibitory control (N2) and error monitoring (error-related negativity). Questions emerge regarding the similarity of attention regulatory difficulties in PIs to those experienced by non-PI children with ADHD.

ASSOCIATIONS BETWEEN DISPOSITIONS TO RASH ACTION AND INTERNALIZING AND EXTERNALIZING SYMPTOMS IN CHILDREN.

Marmorstein NR.

Impulsivity is not a unitary construct; instead, dispositions to rash action can be divided into five moderately-correlated dimensions. However, the associations between these dimensions and symptoms of psychopathology among youth remain unclear. The goal of this study was to examine associations between different dispositions to rash action and psychopathology in a community sample of middle school youth. One hundred forty-four youth (M age = 11.9; 65% Hispanic, 30% African American; 50% male; 81% qualifying for free school lunches) participated in this study. Self-reported questionnaire measures of dispositions to rash action (lack of planning, lack of perseverance, sensation seeking, negative urgency, and positive urgency) and psychopathology symptoms (conduct disorder [CD], alcohol use, depression, overall anxiety, panic, generalized anxiety, social anxiety, and separation anxiety, as well as teacher reports of attention deficit/hyperactivity disorder [ADHD] inattentive and hyperactive symptoms) were used. Negative and positive urgency were positively associated with all symptom types examined except certain anxiety subtypes (and positive urgency was not associated with ADHD symptoms). Lack of planning was positively associated with externalizing and depressive symptoms. Lack of perseverance was positively associated with CD. Sensation seeking was positively associated with both CD and alcohol use. When other dispositions were adjusted for, negative urgency remained a positive predictor of CD, whereas positive urgency remained a positive predictor of depressive and panic symptoms. Sensation seeking was negatively associated with separation anxiety. Psychopathology symptoms are differentially related to dispositions to rash action in children; emotion-based dispositions to rash action may be particularly important targets for future research.

TRANSCRANIAL MAGNETIC STIMULATION AT 1 Hertz IMPROVES CLINICAL SYMPTOMS IN CHILDREN WITH TOURETTE SYNDROME FOR AT LEAST 6 MONTHS.


Tourette syndrome (TS) is characterized by multiple motor and phonic tics. Repetitive transcranial magnetic stimulation (rTMS) targeting the supplemental motor area (SMA) can reduce tic severity. Here, we investigated whether 1 Hz rTMS targeted to the SMA could improve symptoms in children with TS. Twenty-five children with TS (aged under 16 years) received 20 daily sessions of rTMS to the SMA at a frequency of 1 Hz, 110% of resting motor threshold (RMT). Clinical assessment and physiological measures of the left and right RMT were conducted at different times during treatment and follow-up. After four weeks of treatment we observed statistically significant reductions on the Yale Global Tic Severity Scale, Clinical Global Impression Scale, Swanson, Nolan and Pelham Rating Scale, version IV for attention-deficit hyperactivity disorder, Children's Depression Inventory, Spence Children's Anxiety Scale.
and a novel Attention Test. In addition, symptom improvement correlated with an increase of both right and left RMT and was stable at six months follow-up. Therefore, we found that 1 Hz rTMS to the SMA can improve clinical symptoms in children with TS for at least six months.


WHY SO MANY EPIDEMICS OF CHILDHOOD MENTAL DISORDER?
Frances A, Batstra L.


THE EFFECT OF PRENATAL METHAMPHETAMINE EXPOSURE ON ATTENTION AS ASSESSED BY CONTINUOUS PERFORMANCE TESTS: RESULTS FROM THE INFANT DEVELOPMENT, ENVIRONMENT, AND LIFESTYLE STUDY.
OBJECTIVE: To assess for the increased risk of attention-deficit hyperactivity disorder (ADHD) in young children with prenatal methamphetamine exposure from the multicenter, longitudinal Infant Development, Environment, and Lifestyle (IDEAL) study.
METHODS: The IDEAL study enrolled 412 mother-infant pairs at 4 sites (Tulsa, OK; Des Moines, IA; Los Angeles, CA; and Honolulu, HI). Methamphetamine-exposed subjects (n=204) were identified by self-report and/or gas chromatography/mass spectrometry confirmation of amphetamine and metabolites in infant meconium. Matched subjects (n=208) denied methamphetamine use and had a negative meconium screen. This analysis included a subsample of 301 subjects who were administered the Conners’ Kiddie Continuous Performance Test (K-CPT) at 5.5 years of age (153 exposed and 148 comparison). Hierarchical linear models adjusted for covariates tested exposure effects on K-CPT measures. Using the same covariates, logistic regression was used to determine the effect of exposure on the incidence of a positive ADHD confidence index score, defined as greater than 50%.
RESULTS: There were no differences between the groups in omission or commission errors or reaction time for correct trials. However, methamphetamine exposure was associated with subtle differences in other outcomes predictive of ADHD, including increased slope of reaction time across blocks (p < .001), increased variability in reaction time with longer interstimulus intervals (p < .01), and increased likelihood of greater than 50% on the ADHD confidence index (odds ratio, 3.1; 95% confidence interval, 1.2-7.8; p=.02).
CONCLUSION: Prenatal methamphetamine exposure was associated with subtle differences in K-CPT scores at 5.5 years of age. Even at this relatively young age, these children exhibit indicators of risk for ADHD and warrant monitoring.


ATTENTION PROBLEMS IN CHILDHOOD AND ADULT SUBSTANCE USE.
Galera C, Pingault JB, Fombonne E, et al.
OBJECTIVE: To assess the link between childhood attention problems (AP) and substance use 18 years later.
STUDY DESIGN: This cohort study was conducted in a community sample of 1103 French youths followed from 1991 to 2009. Exposures and covariates were childhood behavioral problems (based on parental report at baseline), early substance use, school difficulties, and family adversity. Outcome measures were regular tobacco smoking, alcohol problems, problematic cannabis use, and lifetime cocaine use (based on youth reports at follow-up).
RESULTS: Individuals with high levels of childhood AP had higher rates of substance use (regular tobacco smoking, alcohol problems, problematic cannabis use, and lifetime cocaine use). However, when taking into account other childhood behavioral problems, early substance use, school difficulties, and family adversity, childhood AP were related only to regular tobacco smoking and lifetime cocaine use. Early cannabis exposure was the strongest risk factor for all substance use problems.
CONCLUSION: This longitudinal community-based study shows that, except for tobacco and cocaine, the association between childhood AP and substance use is confounded by a range of early risk factors. Early cannabis exposure plays a central role in later substance use.


DEVELOPMENTAL, EMOTIONAL AND BEHAVIORAL CO-MORBIDITIES ACROSS THE CHRONIC HEALTH CONDITION SPECTRUM.
Blackman JA, Conaway MR.
AIMS: Estimate the prevalence of specific developmental, emotional, and behavioral (DEB) problems across selected chronic health conditions; examine the relationship of chronic health conditions to functional activities and participation; determine the potential confounding effect of sociodemographic factors on the prevalence of DEB problems.
METHODS: The 2007 National Survey of Children's Health, conducted by the Centers for Disease Control and Prevention, served as the primary data source for this study. A total of 91,642 interviews (66.6% response rate for identified households with children) were performed. Population-based estimates were obtained for variables of interest by assigning sampling weights to each child for whom an interview was completed.
RESULTS: Parents were two to 30 times more likely to report DEB problems, such as Attention Deficit/Hyperactivity Disorder, depression, learning problems, and challenging behaviors, for children with chronic health conditions. These children had a greater number and range of difficulties with social interaction and school functioning as well as a lower rate of participation in community activities. Although highest rates of DEB problems were reported for those conditions involving the nervous or sensory systems, children with asthma, diabetes, and musculoskeletal conditions also had a higher rate of problems than children without the conditions. The higher prevalence of DEB problems remained after statistical adjustment for socio-demographic factors.
CONCLUSIONS: Children with a spectrum of chronic health conditions are at high risk for DEB problems that affect learning, behavior, and emotional well-being. As part of a comprehensive approach to the management of chronic health conditions, children should be screened for these problems and referred for appropriate further evaluation and remediation. Attention to these common co-morbidities will not only result in enhanced quality of life but will also promote better adherence to medical recommendations and, thereby, optimal disease control.

NON-MEDICAL USE OF PSYCHOTROPIC PRESCRIPTION DRUGS AMONG ADOLESCENTS IN SUBSTANCE USE TREATMENT.
Apantaku-Olajide T, Smyth BP.
Little is known about the extent of non-medical use of prescription drugs among European adolescents with substance use disorders. This cross-sectional study examined non-medical use of seven categories of psychotropic prescription drugs (opioid analgesics, ADHD stimulant, sleeping, sedative/anxiolytic, antipsychotic, antidepressant, and anabolic steroid medications) in a clinical sample of Irish adolescents with substance use disorders. Of the 85 adolescents (aged 13-18 years) invited to participate, 65 adolescents (M=16.3 years, SD=1.3) took part (response: 74%). Among respondents, 68% reported lifetime non-medical use of any of the prescription drugs; sedative/anxiolytic (62%) and sleeping medications (43%) were more commonly abused. The most frequently reported motives for abuse were "seeking high or buzz" (79%), "having good time" (63%), and "relief from boredom" (56%). Sharing among friends and street-level drug markets were the most readily available sources. Innovative solutions of control measures and intervention are required to address the abuse of prescription drugs.
MIDDLE SCHOOL STUDENTS’ WILLINGNESS TO ENGAGE IN ACTIVITIES WITH PEERS WITH ADHD SYMPTOMS: A MULTIPLE INDICATORS MULTIPLE CAUSES (MIMIC) MODEL.
Ogg J, McMahan MM, Dedrick RF, et al.
Researchers examining peers' behavioral intentions toward students diagnosed with ADHD have frequently used vignettes and asked students to indicate their willingness to engage with an individual described either with or without symptoms of ADHD. The Shared Activities Questionnaire (SAQ-B) is one instrument that has been used to measure students' intentions to engage with students represented in these vignettes. Confirmatory factor analysis results from 183 middle school students supported the three-factor model underlying the SAQ-B, although there were some areas of model misfit. To examine the effects of experimentally manipulating two vignette conditions (describing a peer displaying ADHD symptoms or a peer without these symptoms) on students' responses to items on the SAQ-B, a multiple indicators, multiple causes (MIMIC) analysis was used. Results of the MIMIC analyses identified 4 of the 24 SAQ-B items that exhibited statistically significant uniform differential item functioning between the experimental vignette conditions. Comparisons of the latent variable means between experimental conditions indicated that participants expressed greater willingness to engage with a peer without ADHD symptoms than with one with symptoms on academic activities; no differences were found on the latent variable means for social and recreational activities. Familiarity with ADHD did not have a significant relation to participants’ willingness to engage in any of the three types of activities. Implications for practice and research are discussed.

ADOLESCENT CAFFEINE CONSUMPTION AND SELF-REPORTED VIOLENCE AND CONDUCT DISORDER.
Kristjansson AL, Sigfusdottir ID, Frost SS, et al.
Caffeine is the most widely used psychoactive substance in the world and currently the only one legally available to children and adolescents. The sale and use of caffeinated beverages has increased markedly among adolescents during the last decade. However, research on caffeine use and behaviors among adolescents is scarce. We investigate the relationship between adolescent caffeine use and self-reported violent behaviors and conduct disorders in a population-based cross-sectional sample of 3,747 10th grade students (15-16 years of age, 50.2 % girls) who were enrolled in the Icelandic national education system during February 2012. Through a series of multiple regression models, while controlling for background factors, Attention Deficit Hyperactivity Disorder symptoms and current medication and peer delinquency, and including measures on substance use, our findings show robust additive explanatory power of caffeine for both violent behaviors and conduct disorders. In addition, the association of caffeine to the outcomes is significantly stronger for girls than boys for both violent behaviors and conduct disorders. Future studies are needed to examine to what extent, if at all, these relationships are causal. Indication of causal connections between caffeine consumption and negative outcomes such as those reported here would call into question the acceptability of current policies concerning the availability of caffeine to adolescents and the targeting of adolescence in the marketing of caffeine products.

JAMA Psychiatry. 2013 Nov;70:1231-40.
PRETERM BIRTH AND MORTALITY AND MORBIDITY: A POPULATION-BASED QUASI-EXPERIMENTAL STUDY.
D’Onofrio BM, Class QA, Rickert ME, et al.
IMPORTANCE: Preterm birth is associated with increased mortality and morbidity. However, previous studies have been unable to rigorously examine whether confounding factors cause these associations rather than the harmful effects of being born preterm.
OBJECTIVE: To estimate the extent to which the associations between early gestational age and offspring mortality and morbidity are the result of confounding factors by using a quasi-experimental design, the sibling-comparison approach, and by controlling for statistical covariates that varied within families.
DESIGN, SETTING, AND PARTICIPANTS: A population-based cohort study, combining Swedish registries to identify all individuals born in Sweden from 1973 to 2008 (3,300,708 offspring of 1,736,735 mothers) and link them with multiple outcomes.

MAIN OUTCOMES AND MEASURES: Offspring mortality (during infancy and throughout young adulthood) and psychiatric (psychotic or bipolar disorder, autism, attention-deficit/hyperactivity disorder, suicide attempts, substance use, and criminality), academic (failing grades and educational attainment), and social (partnering, parenthood, low income, and social welfare benefits) outcomes through 2009.

RESULTS: In the population, there was a dose-response relationship between early gestation and the outcome measures. For example, extreme preterm birth (23-27 weeks of gestation) was associated with infant mortality (odds ratio, 288.1; 95% CI, 271.7-305.5), autism (hazard ratio [HR], 3.2; 95% CI, 2.6-4.0), low educational attainment (HR, 1.7; 1.5-2.0), and social welfare benefits (HR, 1.3; 1.2-1.5) compared with offspring born at term. The associations between early gestation and mortality and psychiatric morbidity generally were robust when comparing differentially exposed siblings and controlling for statistical covariates, whereas the associations with academic and some social problems were greatly or completely attenuated in the fixed-effects models.

CONCLUSIONS AND RELEVANCE: The mechanisms responsible for the associations between preterm birth and mortality and morbidity are outcome-specific. Associations between preterm birth and mortality and psychiatric morbidity are largely independent of shared familial confounds and measured covariates, consistent with a causal inference. However, some associations, particularly predicting suicide attempt, educational attainment, and social welfare benefits, are the result of confounding factors. The findings emphasize the importance of both reducing preterm birth and providing wraparound services to all siblings in families with an offspring born preterm.


DISORGANIZATION AS RELATED TO DISEORDINATION AND ATTENTION DEFICIT.
Lifshitz N, Josman N, Tirosh E.

Our objective was to examine the association of attention deficit and disorganization in boys with and without specific developmental disorder of motor function. Four groups of boys between the age of 7 and 12 years - (1) Disorganization + coordination disorder (n=30); (2) Coordination disorder (n=33); (3) Disorganization (n=28); and (4) Control (n=29) - were included. Teachers completed the Questionnaire for Assessing the Students' Organizational Abilities for the Teacher and the Conners' Teachers Rating Scale-Revised. The Movement Assessment Battery for Children and 2 subscales of an intelligence test (vocabulary and similarities) were administered. A significantly increased rate of attention deficit in children with organizational deficit was identified. Attention deficit in children with specific motor disorder was exclusively associated with an organizational deficit. Organizational deficit in childhood is highly associated with attention deficit, and this association is particularly relevant in children with specific coordination disorder.


CLINICAL OBSERVATIONS ON ATTENTION-DEFICIT HYPERACTIVITY DISORDER (ADHD) IN CHILDREN WITH FRONTAL LOBE EPILEPSY.
Zhang DQ, Li FH, Zhu XB, et al.

The objective was to investigate the prevalence of attention-deficit hyperactivity disorder (ADHD) in children with frontal lobe epilepsy and related factors. The medical records of 190 children diagnosed with frontal lobe epilepsy at Qilu Hospital of Shandong University between 2006 and 2011 were retrospectively collected, and a follow-up analysis of the prevalence of ADHD in these children was conducted. Of the 161 children with an effective follow-up, 59.0% (95/161) with frontal lobe epilepsy suffered from ADHD as well. Analysis of epilepsy and ADHD-related factors indicated that the incidence of ADHD was 89.4% (76/85) in children with abnormal electroencephalogram (EEG) discharges on the most recent EEG, which was significantly higher than the ADHD incidence of 25% (19/76) in children with normal readings on the most
recent EEG (P < .01). Children with frontal lobe epilepsy have a high incidence of ADHD. Sustained
abnormal discharge on the electroencephalogram is associated with increased comorbidity of ADHD with
frontal lobe epilepsy.

FAMILIAL CONFOUNDING OF THE ASSOCIATION BETWEEN MATERNAL SMOKING DURING PREGNANCY AND ADHD IN
OFFSPRING.
Skoglund C, Chen Q, D’Onofrio BM, et al.
Background: Maternal Smoking During Pregnancy (SDP) has consistently been associated with increased
risk of attention-deficit/hyperactivity disorder (ADHD) in offspring, but recent studies indicate that this
association might be due to unmeasured familial confounding.
Methods: A total of 813,030 individuals born in Sweden between 1992 and 2000 were included in this
nationwide population-based cohort study. Data on maternal SDP and ADHD diagnosis were obtained from
national registers and patients were followed up from the age of 3 to the end of 2009. Hazard Ratios (HRs)
were estimated using stratified Cox regression models. Cousin and sibling data were used to control for
unmeasured familial confounding.
Results: At the population level maternal SDP predicted ADHD in offspring (HR[sub ModerateSDP]/[sub] =
1.89; HR[sub HighSDP]/[sub] = 2.50). This estimate gradually attenuated toward the null when adjusting for
measured confounders (HR[sub ModerateSDP]/[sub] = 1.62; HR[sub HighSDP]/[sub] = 2.04), unmeasured
confounders shared within the extended family (i.e., cousin comparison) (HR[sub ModerateSDP]/[sub] =
1.45; HR[sub HighSDP]/[sub] = 1.69), and unmeasured confounders within the nuclear family (i.e., sibling
comparison) (HR[sub ModerateSDP]/[sub] = 0.88; HR[sub HighSDP]/[sub] = 0.84).
Conclusions: Our results suggest that the association between maternal SDP and offspring ADHD are
due to unmeasured familial confounding.

LONG-TERM EFFECTS OF ADHD MEDICATION ON ADULT HEIGHT: RESULTS FROM THE NESARC.
Peyre H, Hoertel N, Cortese S, et al.

FOOD ADDITIVES AND BEHAVIOR IN 8- TO 9-YEAR-OLD CHILDREN IN HONG KONG: A RANDOMIZED, DOUBLE-BLIND,
PLACEBO-CONTROLLED TRIAL.
Lok KYW, Chan RSM, Lee VVY, et al.
Objectives: To test the individual effect of artificial food colorings (AFCs) and a preservative on the
behavior of the general Chinese population.
Method: One hundred thirty children (70 boys and 60 girls) in Hong Kong with a mean age of 8.64 years
were enlisted to the study with a within-subject crossover between AFCs, a preservative (sodium
benzoate), and a placebo capsule. Two behavior scores were used including the strengths and
weaknesses of attention deficit hyperactivity disorder and normal behavior rating scale and the child
behavior checklist-teacher report form.
Results: Capsule A containing AFCs and Capsule B containing sodium benzoate had no significant
adverse effect compared with placebo in both behavior scores. This result persisted when analysis was
restricted to children with 85% consumption of capsule (per protocol analysis).
Conclusion: There seem to be no significant associations between AFCs and a preservative on Chinese children’s behavior at the age of 8 to 9 years. Future directions and implications of this research are discussed.


ELECTROENCEPHALOGRAPHY CORRELATES OF SPATIAL WORKING MEMORY DEFICITS IN ATTENTION-DEFICIT/HYPERACTIVITY DISORDER: VIGILANCE, ENCODING, AND MAINTENANCE.


In the current study we sought to dissociate the component processes of working memory (WM) (vigilance, encoding and maintenance) that may be differentially impaired in attention-deficit/hyperactivity disorder (ADHD). We collected electroencephalographic (EEG) data from 52 children with ADHD and 47 typically developing (TD) children, ages 7-14 years, while they performed a spatial Sternberg working memory task. We used independent component analysis and time-frequency analysis to identify midoccipital alpha (8-12 Hz) to evaluate encoding processes and frontal midline theta (4-7 Hz) to evaluate maintenance processes. We tested for effects of task difficulty and cue processing to evaluate vigilance. Children with ADHD showed attenuated alpha band event-related desynchronization (ERD) during encoding. This effect was more pronounced when task difficulty was low (consistent with impaired vigilance) and was predictive of memory task performance and symptom severity. Correlated with alpha ERD during encoding were alpha power increases during the maintenance period (relative to baseline), suggesting a compensatory effort. Consistent with this interpretation, midfrontal theta power increases during maintenance were stronger in ADHD and in high-load memory conditions. Furthermore, children with ADHD exhibited a maturational lag in development of posterior alpha power whereas age-related changes in frontal theta power deviated from the TD pattern. Last, subjects with ADHD showed age-independent attenuation of evoked responses to warning cues, suggesting low vigilance. Combined, these three EEG measures predicted diagnosis with 70% accuracy. We conclude that the interplay of impaired vigilance and encoding in ADHD may compromise maintenance and lead to impaired WM performance in this group.


REWARD AND PUNISHMENT SENSITIVITY ARE DIFFERENTIALLY ASSOCIATED WITH ADHD AND SLUGGISH COGNITIVE TEMPO SYMPTOMS IN CHILDREN.

Becker SP, Fite PJ, Garner AA, et al.

Research demonstrates that attention-deficit/hyperactivity disorder (ADHD) and sluggish cognitive tempo (SCT) are likely separate constructs, but no study has examined whether personality dimensions are differentially associated with ADHD and SCT. This study tested the hypothesis that sensitivity to reward would be associated with ADHD symptoms whereas sensitivity to punishment would be associated with SCT symptoms. This hypothesis was examined in a community sample of children ages 9–12 (N = 89; 56% male). As expected, sensitivity to reward (and impulsivity/fun seeking specifically) was associated with ADHD and broadband externalizing symptoms, whereas sensitivity to punishment (and Fear/Shyness specifically) was associated with SCT and broadband internalizing symptoms. Although preliminary, these results suggest that distinct personality dimensions may contribute to the presence of ADHD/externalizing or SCT/internalizing symptoms.


CAN CHILDREN WITH CALLOUS AND UNEMOTIONAL TRAITS BE TREATED SUCCESSFULLY?

Newcorn JH.

Comments on an article by Joseph C. Blader et al. (see record 2013-42904-012). In the study, the authors conducted an open stimulant optimization protocol as part of a larger study of youth with attention deficit/hyperactivity disorder (ADHD) and aggression. The group was well assessed with regard to ADHD,
aggression, aggression subtypes, and callous and unemotional (CU) traits using state-of-the-art measurements. The main study findings are that pretreatment ratings of CU traits and proactive aggression did not negatively predict remission of aggression; children whose aggression remitted had a decrease in CU traits and proactive aggression. The study presents secondary analyses that examined potential moderating effects of pretreatment CU traits and proactive aggression on stimulant treatment of aggression. The investigators provide an excellent review of aggression subtypes and their relation to impulsivity and CU traits and a thoughtful discussion of the study results. The main issue they struggle with is the seemingly counterintuitive finding that children with ADHD and CU traits did not fare worse with stimulant treatment than those without. It is hoped that development of external validators of clinical diagnosis and biomarker-driven treatment approaches will help resolve some of the issues raised by this interesting and very well-done study.


A FOLLOW-UP STUDY OF MATERNAL EXPRESSED EMOTION TOWARD CHILDREN WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER (ADHD): RELATION WITH SEVERITY AND PERSISTENCE OF ADHD AND COMORBIDITY.

Richards JS, Vasquez AA, Rommelse NNJ, et al.

Objective: Attention-deficit/hyperactivity disorder (ADHD) is associated with conflicted parent-child relationships. The underlying mechanisms of this association are not yet fully understood. We investigated the cross-sectional and longitudinal relationships between externalizing psychopathology in children with ADHD, and expressed emotion (EE; warmth and criticism) and psychopathology in mothers.

Method: In this 6-year follow-up study, 385 children with an ADHD combined subtype were included at baseline (mean, 11.5 years, 83.4% male), of which 285 children (74%) were available at follow-up (mean, 17.5 years, 83.5% male). At both time points, measures of child psychopathology (i.e., ADHD severity, oppositional, and conduct problems), maternal EE, and maternal psychopathology (i.e., ADHD and affective problems) were obtained.

Results: EE was not significantly correlated over time. At baseline, we found a nominally negative association (p (less-than or equal to) .05) between maternal warmth and child ADHD severity. At follow-up, maternal criticism was significantly associated with child oppositional problems, and nominally with child conduct problems. Maternal warmth was nominally associated with child oppositional and conduct problems. These associations were independent of maternal psychopathology. No longitudinal associations were found between EE at baseline and child psychopathology at follow-up, or child psychopathology at baseline and EE at follow-up.

Conclusions: The results support previous findings of cross-sectional associations between parental EE and child psychopathology. This, together with the finding that EE was not stable over 6 years, suggests that EE is a momentary state measure varying with contextual and developmental factors. EE does not appear to be a risk factor for later externalizing behavior in children with ADHD.
Anon.  

**BACKGROUND:** Findings from family and twin studies suggest that genetic contributions to psychiatric disorders do not in all cases map to present diagnostic categories. We aimed to identify specific variants underlying genetic effects shared between the five disorders in the Psychiatric Genomics Consortium: autism spectrum disorder, attention deficit-hyperactivity disorder, bipolar disorder, major depressive disorder, and schizophrenia.

**METHODS:** We analysed genome-wide single-nucleotide polymorphism (SNP) data for the five disorders in 33,332 cases and 27,888 controls of European ancestry. To characterise allelic effects on each disorder, we applied a multinomial logistic regression procedure with model selection to identify the best-fitting model of relations between genotype and phenotype. We examined cross-disorder effects of genome-wide significant loci previously identified for bipolar disorder and schizophrenia, and used polygenic risk-score analysis to examine such effects from a broader set of common variants. We undertook pathway analyses to establish the biological associations underlying genetic overlap for the five disorders. We used enrichment analysis of expression quantitative trait loci (eQTL) data to assess whether SNPs with cross-disorder association were enriched for regulatory SNPs in post-mortem brain-tissue samples.

**FINDINGS:** SNPs at four loci surpassed the cutoff for genome-wide significance ($p<5\times10^{-8}$) in the primary analysis: regions on chromosomes 3p21 and 10q24, and SNPs within two L-type voltage-gated calcium channel subunits, CACNA1C and CACNB2. Model selection analysis supported effects of these loci for several disorders. Loci previously associated with bipolar disorder or schizophrenia had variable diagnostic specificity. Polygenic risk scores showed cross-disorder associations, notably between adult-onset disorders. Pathway analysis supported a role for calcium channel signalling genes for all five disorders. Finally, SNPs with evidence of cross-disorder association were enriched for brain eQTL markers.

**INTERPRETATION:** Our findings show that specific SNPs are associated with a range of psychiatric disorders of childhood onset or adult onset. In particular, variation in calcium-channel activity genes seems to have pleiotropic effects on psychopathology. These results provide evidence relevant to the goal of moving beyond descriptive syndromes in psychiatry, and towards a nosology informed by disease cause.

**FUNDING:** National Institute of Mental Health.

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**Iron Deficiency After Arrival Is Associated With General Cognitive and Behavioral Impairment in Post-institutionalized Children Adopted From Eastern Europe.**


To investigate the role of iron deficiency in general cognitive and behavioral development in post-institutionalized (PI) children during the early post-adoption period. PI children (N = 57) adopted from Eastern Europe or Central Asia (9-46 months of age) were seen at baseline around 1 month after arrival into the US and at follow-up 6 months later. Measures included anthropometry, iron status, the Toddler Behavior Assessment Questionnaire-R (TBAQ-R), the Mullen Scales of Early Learning, and examiner-rated behaviors during testing. 26 % were iron deficient at baseline; 18 % were iron deficient at follow-up. There was a trend for those with iron deficiency at baseline to be more fearful on the TBAQ-R. Those with iron deficiency at follow-up displayed more hyperactivity on both the TBAQ-R and the examiner-rated behaviors. Those with iron deficiency at follow-up were more likely to score below average on the Mullen Early Learning Composite (iron deficient: 80 %; good iron status: 32 %). The association between iron status at follow-up and the Mullen Early Learning Composite was mediated by inattention and hyperactivity behaviors during testing. Iron deficiency is associated with neurobehavioral alterations months after arrival, mediated by the effect on attention and activity levels. Iron status needs to be monitored at least through the first half-year post-adoption, particularly in children exhibiting rapid catch-up growth. Additionally,
**PARENTAL DEPRESSIVE SYMPTOMS AND CHILDREN’S SCHOOL ATTENDANCE AND EMERGENCY DEPARTMENT USE: A NATIONALLY REPRESENTATIVE STUDY.**


We sought to assess the association between parental depressive symptoms and school attendance and emergency department (ED) use among children with and without chronic health conditions. Secondary analysis of the 1997-2004 National Health Interview Survey, a nationally representative survey. Parental depressive symptoms were measured by three questions assessing sadness, hopelessness, or worthlessness in the past month. Children with and without asthma or attention-deficit/hyperactivity disorder (ADHD) were identified, and their school attendance and ED visits were reported by adult household respondents. Children with information on parental depressive symptoms, health conditions, and services use were eligible. We incorporated weights available in the survey for each eligible child to reflect the complex sampling design. 104,930 eligible children were identified. The point prevalence of parental depressive symptoms was low (1.8 %, 95 % CI 1.7-2.0), but greater among children with asthma (2.7 %, 95 % CI 2.4-3.0) and ADHD (3.8 %, 95 % CI 3.2-4.4) than among other children (1.6 %, 95 % CI 1.5-1.7). After adjustment for potential confounders, children whose parents reported depressive symptoms most or all of the time were more likely to report an ED visit (adjusted incident rate ratio [IRR] 1.18, 95 % CI 1.06-1.32) or school absence (adjusted IRR 1.36, 95 % CI 1.14-1.63) than children whose parents did not. The effect of parental depressive symptoms was not modified by child health conditions. Parental depressive symptoms were adversely associated with school attendance and ED use in children. These results suggest the importance of measuring depressive symptoms among adult caregivers of children.

**GENOME-WIDE ANALYSIS OF RARE COPY NUMBER VARIATIONS REVEALS PARK2 AS A CANDIDATE GENE FOR ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.**

Jarick I, Volckmar AL, Putter C, et al.

Attention-deficit/hyperactivity disorder (ADHD) is a common, highly heritable neurodevelopmental disorder. Genetic loci have not yet been identified by genome-wide association studies. Rare copy number variations (CNVs), such as chromosomal deletions or duplications, have been implicated in ADHD and other neurodevelopmental disorders. To identify rare (frequency (less-than or equal to)1%) CNVs that increase the risk of ADHD, we performed a whole-genome CNV analysis based on 489 young ADHD patients and 1285 adult population-based controls and identified one significantly associated CNV region. In tests for a global burden of large (>500 kb) rare CNVs, we observed a nonsignificant (P=0.271) 1.126-fold enriched rate of subjects carrying at least one such CNV in the group of ADHD cases. Locus-specific tests of association were used to assess if there were more rare CNVs in cases compared with controls. Detected CNVs, which were significantly enriched in the ADHD group, were validated by quantitative (q)PCR. Findings were replicated in an independent sample of 386 young patients with ADHD and 781 young population-based healthy controls. We identified rare CNVs within the parkinson protein 2 gene (PARK2) with a significantly higher prevalence in ADHD patients than in controls (P=2.8 null 10 -4 after empirical correction for genome-wide testing). In total, the PARK2 locus (chr 6: 162 659 756-162 767 019) harboured three deletions and nine duplications in the ADHD patients and two deletions and two duplications in the controls. By qPCR analysis, we validated 11 of the 12 CNVs in ADHD patients (P=1.2 null 10 -3 after empirical correction for genome-wide testing). In the replication sample, CNVs at the PARK2 locus were found in four additional ADHD patients and one additional control (P=4.3 null 10 -2). Our results suggest that copy number variants at the PARK2 locus contribute to the genetic susceptibility of ADHD. Mutations and CNVs in PARK2 are known to be associated with Parkinson disease.
Most psychiatric disorders are moderately to highly heritable. The degree to which genetic variation is unique to individual disorders or shared across disorders is unclear. To examine shared genetic etiology, we use genome-wide genotype data from the Psychiatric Genomics Consortium (PGC) for cases and controls in schizophrenia, bipolar disorder, major depressive disorder, autism spectrum disorders (ASD) and attention-deficit/hyperactivity disorder (ADHD). We apply univariate and bivariate methods for the estimation of genetic variation within and covariation between disorders. SNPs explained 17-29% of the variance in liability. The genetic correlation calculated using common SNPs was high between schizophrenia and bipolar disorder (0.68 +/- 0.04 s.e.), moderate between schizophrenia and major depressive disorder (0.43 +/- 0.06 s.e.), bipolar disorder and major depressive disorder (0.47 +/- 0.06 s.e.), and ADHD and major depressive disorder (0.32 +/- 0.07 s.e.), low between schizophrenia and ASD (0.16 +/- 0.06 s.e.) and non-significant for other pairs of disorders as well as between psychiatric disorders and the negative control of Crohn's disease. This empirical evidence of shared genetic etiology for psychiatric disorders can inform nosology and encourages the investigation of common pathophysiologies for related disorders.

EVIDENCE OF AN ASSOCIATION BETWEEN 10/10 GENOTYPE OF DAT1 AND ENDOPHENOTYPES OF ATTENTION DEFICIT/HYPERACTIVITY DISORDER.

Agudelo JA, Galvez JM, Fonseca DJ, et al.

Introduction: Genetic variance of attention deficit-hyperactivity disorder (ADHD) is a strong determinant of this disorder. The 40 base pairs (bp) variable number tandem repeat (VNTR) located in the 3' untranslated region (UTR) of DAT1 gene increases the expression of the dopamine transporter. Therefore, DAT1 has been associated with susceptibility to ADHD.

Objective: To determine the association between the VNTR of DAT1 and the phenotype of ADHD or its endophenotypes in a sample of children aged between 6 and 15 years from Bogota.

Subjects and methods: We selected 73 patients with ADHD and 54 controls. WISC test was applied in all subjects and executive functions were assessed. The VNTR of DAT1 was polymerase chain reaction-amplified. Data regarding population genetics and statistical analysis were obtained. Correlation and association tests between genotype and neuropsychological testing were performed.

Results: The DAT1 polymorphism was not associated with ADHD (P=.85). Nevertheless, the 10/10 genotype was found to be correlated with the processing speed index (P<.05). In the hyperactivity subtype, there was a genotypic correlation with some subtests of executive function (cognitive flexibility) (P(less-than or equal to).01). In the combined subtype, the 10/10 genotype was associated with verbal comprehension index of WISC (P<.05).

Conclusions: A correlation was found between DAT1 VNTR and the subtest "processing speed index" of WISC and the subtest "cognitive flexibility" of executive functions. To our knowledge, this is the first report to assess DAT1 gene in a Colombian population.

PHARMACOGENETICS OF GROWTH EFFECTS COMPLICATING ADHD TREATMENT.


Background: Pharmacogenetics matches individuals with optimal treatment based on genetic background and can identify individuals at risk for adverse medication events. However, psychiatric pharmacogenetics lags behind other areas of medicine. Previously we reported monoaminergic variants influencing treatment response to methylphenidate and guanfacine in children and adolescents with ADHD in the UCLA Translational Research to Enhance Cognitive Control (TRECC) sample. We now report pharmacogenetic influences on stimulant-mediated growth slowing. Growth effects of ADHD pharmacotherapies are.
important, treatment-limiting side effects. Due to monoamine and acetylcholine involvement in growth hormone regulation and energy balance, we examined genetic variation in these signaling pathways for association with growth effects.

**Methods**: 202 subjects between 7-14 years of age were recruited for the acute phase of a randomized, double-blind, placebo-controlled trial of dexmethylphenidate (d-MPH) and guanfacine for pediatric ADHD. Three treatment groups included guanfacine monotherapy, d-MPH monotherapy, and combination guanfacine plus d-MPH. Medication responders continued in the trial for approximately 14 months (n=99) and height and weight were tracked regularly in addition to ADHD symptoms. We tested association of genetic variation in monoamine and energy balance candidate systems with height and BMI changes during medication exposure. Complete common variation was captured across dopaminergic (DRD1-5), adrenergic (ADRA2A, SLC6A2, HCN1), serotonergic (SLC6A4, HTR2C), cholinergic (CHRNA3, A4, A5, A7, CHRN2B), monoamine catabolic enzyme (MAO-A, MAO-B), and energy balance (FTO, LEP, NPY, MC3R, MC4R, CNR1) pathways. A generalized linear mixed model (GLMM) was used to analyze the three-way interaction of treatment group by genotype by time on change in height (Z-score) and BMI (Z-score). Since small non-Caucasian group sizes could produce unstable effects, we limited our analyses to the Caucasian subset (n=147). Due to the large number of markers tested (n=95), we only report results meeting genomewide significance.

**Results**: In our sample, guanfacine monotherapy was associated with height and BMI acceleration compared to that predicted from CDC growth charts (Z-score increase of 0.14 for height and 0.41 for BMI). Both d-MPH monotherapy (Z-score decrease of -0.12 for height and -0.84 for BMI) and combination treatment (Z-score decrease of -0.19 for height and -0.83 for BMI) were associated with growth slowing. Overall, variation in treatment group trajectories for height (p=6.47null10-15) and BMI (p=5.58null10-34) were highly significant. Variants in the cannabinoid receptor CNR1 (rs806378 p=2.68null10-9); the norepinephrine transporter SLC6A2 (rs36021 p=2.29null10-15); the serotonin transporter SLC6A4 (rs4251417 p=3.75null10-9); the dopamine DRD2 receptor (rs1079596 p=1.49null10-9, rs6277 p=1.96null10-9); and cholinergic receptors CHRNA4 (rs2236196 p=5null10-8), CHRNA5 (rs16969968 p=1.96null10-19) and CHRNA7 (rs6494212 p=2.51null10-8, rs711 p=6.00null10-9) were associated with height but not BMI change across all 3 treatment conditions. Effects specific to treatment condition were apparent. Individuals homozygous for the common allele of DRD4 rs3758653 treated with guanfacine monotherapy showed a 0.6 increase in height z-score compared to minor allele carriers (p=5.54null10-9), while no genetic effects were present in MPH+ groups. Conversely, in the MPH-only condition, DRD3 rs3732790 minor allele homozygotes showed a 2.0 greater z-score weight loss then common allele carriers (p=1.09null10-8), while no genetic effects were present in guanfacine + groups. Surprisingly, minor allele homozygotes at DRD1 rs4867798 demonstrated greater height gain than predicted in both MPH+ conditions, but the guanfacine monotherapy group (p=8.32null10-21). Homozygotes for the common allele at ADRA2A rs3750625 (p=1.62null10-8) and the rare allele at DRD3 rs2134655 (p=2.18null10-9) revealed opposite height effects in guanfacine and MPH conditions. Negative effects of multiple NPY alleles on height change were predominantly seen in the combination condition (rs16147 p=9.67null10-10, rs16141 p=4.02null10-10, rs3905497 p=7.33null10-17, rs16148 p=3.98null10-14).

**Conclusions**: The power afforded by a repeated measures model across 16 months of visits would allow us to detect even small effects of guanfacine and stimulant treatment on growth. However, effect sizes between alleles are consistently in the moderate to strong range. Rare variants with extreme height effects in CHRNA4, CHRNA5, and DRD3 certainly require replication in larger samples, but are supported by functional data for variant effects on receptor signaling. Interestingly, the alleles associated with treatment response in our prior analyses were also associated with growth effects here, supporting a hypothesis of allele-specific increases in drug sensitivity. We are currently exploring methods for combining genetic factors to produce clinically actionable pharmacogenetic-based treatment recommendations. The results presented here suggest that genetic factors contribute significantly to stimulant-mediated growth slowing and are able to identify patients likely to be affected. Choice of optimal treatment in the future can be guided by both response and side effect pharmacogenetics.
ALTERATIONS IN AMYGDALA FUNCTIONAL CIRCUITRY AS A NEURAL MARKER OF EMOTION DYSREGULATION IN YOUNG CHILDREN.

Ring AK, Klein RG, Kelly C, et al.

Background: A great deal of controversy has surrounded the diagnosis of children with severe, impairing temper outbursts. Some claim that such outbursts reflect a juvenile form of bipolar disorder, with significant implications for prognosis and treatment. We recently found that most young children (5-9 years old) with extreme outbursts, defined as relatively long and frequent, are most often diagnosed with Attention-Deficit/Hyperactivity Disorder (ADHD) and/or Oppositional Defiant Disorder (ODD), and not bipolar disorder (Roy et al, in press). Some of these children also suffer from chronic irritability or negative mood that does not fit easily into extant DSM-IV categories. In an effort to improve the reliable diagnosis of these youth, DSM-5 established a new diagnosis, Disruptive Mood Dysregulation Disorder (DMDD). In light of increased interest in utilizing biomarkers of behavioral phenotypes to inform, and improve, nosology, the present study uses resting state functional MRI to assess emotion regulation circuitry in young children who exhibit severe temper outbursts. Given the high prevalence of ADHD in this population, we include a psychiatric comparison group of children with ADHD without temper outbursts, as well as a healthy comparison group. We hypothesize that amygdala-frontal circuits involved in emotion regulation will be altered in children with extreme outbursts, as compared to both comparison groups.

Methods: Data collection is ongoing. Three groups of children (ages 5-9 years) were recruited: (1) Children with severe, impairing temper outbursts (in excess of 10 min at least 3 times per week; TO group; n=23); (2) children with ADHD without significant temper outbursts (ADHD group; n=25); and (3) healthy children with no psychiatric concerns (HC group; n=15). Participants completed a clinical evaluation including the K-SADS-PL and measures of emotion regulation. Following this assessment, eligible participants completed an MRI scan session including a 6-min rest scan (e.g., lie still with eyes open) and a high resolution anatomical scan for registration purposes. Whole-brain analyses were similar to those used in prior studies of amygdala functional connectivity (e.g., Roy et al, 2013). For these initial analyses, we analyzed the intrinsic functional connectivity (iFC) of the total left and right amygdala. A time series was obtained for each ROI and correlations were calculated between these time series and every other voxel in the brain, resulting in individual correlation maps which were then converted to Z-value maps using Fisher's r-to-z transformation, and transformed into MNI152 2mm standard space. Group comparisons were conducted using FLAME, a mixed-effects model implemented in FSL, controlling for age, gender, mean framewise displacement (participant motion), and the scan used (first or second within the session).

Results: Groups did not differ in age, sex, or movement during the resting state scan. All but one child in the TO group were diagnosed with ADHD and the distribution of ADHD type (73.9% Combined Type, 13% Predominantly Hyperactive Type, and 8.7% Predominantly Inattentive Type) did not differ significantly from the ADHD comparison group. DMDD was only diagnosed in five children from the TO group; most did not exhibit chronic irritability. Group comparisons of amygdala iFC yielded two significant findings. First, the TO group showed negative iFC between right amygdala and frontal pole; the ADHD and HC groups showed no significant iFC between these regions. Second, iFC between amygdala and precuneus was negative in the TO group, and positive in the ADHD and HC comparison groups. Overall, the TO group showed significant differences in right amygdala iFC while the two comparison groups did not differ.

Conclusions: These findings provide preliminary evidence of a putative pathophysiological mechanism of emotion dysregulation in children that is not a function of ongoing ADHD. Specifically, young children with severe outbursts, most of whom have ADHD, exhibit alterations in amygdala iFC with regions of the frontal pole and precuneus that are not observed in children with ADHD without such outbursts. Due to the low number of DMDD diagnoses, we were unable to examine how amygdala circuitry may be different for children with temper outbursts with chronic irritability compared to those with outbursts alone. Further study is needed to directly examine this question.
Attention deficit/hyperactivity disorder (ADHD) is the most commonly diagnosed neurobehavioral disorder of childhood. The etiopathogenesis of ADHD has not been totally defined. Recent reports have suggested a pathophysiological role of neurotrophins in ADHD. In this study, we evaluated serum levels of nerve growth factor (NGF) in patients with ADHD. The sample population consisted of 44 child or adolescent patients diagnosed with ADHD according to DSM-IV criteria; 36 healthy subjects were included in the study as controls. Venous blood samples were collected, and NGF levels were measured. The mean serum NGF levels of the ADHD patients were significantly higher than those of the controls. Age and gender of the patients were not correlated with serum NGF levels. There were no significant differences in NGF levels among the combined and predominantly inattentive subtypes of ADHD. Our study suggests that there are higher levels of serum NGF in drug naive ADHD patients, and that increased levels of NGF might have an important role in the pathophysiology of ADHD.

PREVALENCE OF SMOKING, ALCOHOL AND SUBSTANCE USE AMONG ADOLESCENTS WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER IN DENMARK COMPARED WITH THE GENERAL POPULATION.

Madsen AG, Dalsgaard S.

Background: Studies have shown that adolescents with attention-deficit/ hyperactivity disorder (ADHD) have an increased risk of alcohol and substance abuse in adulthood. An unequivocal reason for this association has not yet been identified but it has been shown that pharmacological treatment is likely to reduce this risk.

Aims: To test whether adolescents with ADHD in pharmacological treatment have a higher prevalence of smoking and use of alcohol and drugs than a matched control group from the general population. The study will also analyse associations between smoking, alcohol and drug use and comorbid psychiatric symptoms.

Methods: The sample in this case-control study comprised 219 adolescents aged 13-18 years, including a case group of 117 adolescents with ADHD and a control group of 102 adolescents without ADHD. Participating subjects completed a questionnaire about their use of cigarettes, drugs and alcohol and the self-report version of the Strengths and Difficulties Questionnaire (SDQ).

Results: 21% of ADHD probands vs. 16% controls were daily smokers (P=0.326). Among alcohol users, 52% of ADHD probands vs. 70% controls confirmed monthly alcohol intake (P=0.014); 4% of cases compared with 7% of controls used illicit drugs within last month (P=0.260).

Conclusion: No significant group differences were found in the prevalence of ever having smoked cigarettes, drinking alcohol or using illicit drugs between adolescents with ADHD and controls. Contrary to expectations, subjects in the control group had a more regular and heavier use of alcohol. However, ADHD patients had a heavier use of cigarettes than controls.
were conducted with the categorical diagnosis of ADHD as well as behavioral and cognitive phenotypes related to ADHD. Furthermore, stratified FBAT analyses based on maternal smoking during pregnancy (MSDP) status were conducted.

**Results** Statistically significant associations were observed between rs8050136 and several of the traits tested in the total sample. These associations were stronger when the analysis was restricted to children who were not exposed to MSDP.

**Conclusions** These exploratory results suggest the involvement of the FTO SNP rs8050136 in modulating the risk for ADHD, particularly in those children who were not exposed to MSDP. If confirmed, they may explain, at least in part, the complex links between obesity and ADHD.

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**Prenatal Testosterone and Preschool Disruptive Behavior Disorders.**

Roberts BA, Martel MM.

Disruptive Behavior Disorders (DBD), including Oppositional-Defiant Disorder (ODD) and Attention-Deficit/Hyperactivity Disorder (ADHD), are fairly common and highly impairing childhood behavior disorders that can be diagnosed as early as preschool. Prenatal exposure to testosterone may be particularly relevant to these early-emerging DBDs that exhibit a sex-biased prevalence rate favoring males. The current study examined associations between preschool DBD symptom domains and prenatal exposure to testosterone measured indirectly via right 2D:4D finger-length ratios. The study sample consisted of 109 preschool-age children between ages 3 and 6 (64% males; 72% with DBD) and their primary caregivers. Primary caregivers completed a semi-structured interview (i.e., Kiddie Disruptive Behavior Disorder Schedule), as well as symptom questionnaires (i.e., Disruptive Behavior Rating Scale, Peer Conflict Scale); teachers and/or daycare providers completed symptom questionnaires and children provided measures of prenatal testosterone exposure, measured indirectly via finger-length ratios (i.e., right 2D:4D). Study results indicated a significant association of high prenatal testosterone (i.e., smaller right 2D:4D) with high hyperactive–impulsive ADHD symptoms in girls but not boys, suggesting that the effect may be driven by, or might only exist in, girls. The present study suggests that prenatal exposure to testosterone may increase risk for early ADHD, particularly hyperactivity–impulsivity, in preschool girls.

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**Pharmacol Biochem Behav.** 2013 Jan;103:652-58.

**Rate Dependent Effects of Acute Nicotine on Risk Taking in Young Adults Are Not Related to ADHD Diagnosis.**

Ryan KK, Dube SL, Potter AS.

Beneficial effects of nicotine on cognition and behavioral control are hypothesized to relate to the high rates of cigarette smoking in Attention-Deficit/Hyperactivity Disorder (ADHD). Given that ADHD is associated with both impulsivity and elevated risk taking, we hypothesized that nicotine modulates risk taking, as it does impulsivity. 26 non-smoking young adults (15 controls with normal impulsivity and 11 ADHD with high impulsivity) received 7 mg transdermal nicotine, 20mg oral mecamylamine, and placebo on separate days, followed by the Balloon Analog Risk Task (BART). Statistical analyses found no group differences in baseline risk taking. Reexamination of the data using a median split on baseline risk taking, to create high (HRT) and low (LRT) risk taking groups, revealed significant effects of nicotinic drugs that differed by group. Nicotine reduced risk taking in HRT and mecamylamine increased risk taking in LRT. This finding supports the hypothesis that nicotinic receptor function modulates risk taking broadly, beyond those with ADHD, and is consistent with rate dependent cholinergic modulation of other cognitive functions. Further, the results demonstrate that high impulsivity is separable from high risk taking in young adults with ADHD, supporting the utility of these differential behavioral phenotypes for neurobiological studies.
THE STRENGTHS AND DIFFICULTIES QUESTIONNAIRE AS A PREDICTOR OF PARENT-REPORTED DIAGNOSIS OF AUTISM SPECTRUM DISORDER AND ATTENTION DEFICIT HYPERACTIVITY DISORDER.

Russell G, Rodgers LR, Ford T.

The Strengths and Difficulties Questionnaire (SDQ) is widely used as an international standardised instrument measuring child behaviour. The primary aim of our study was to examine whether behavioral symptoms measured by SDQ were elevated among children with autism spectrum disorder (ASD) and attention deficit hyperactivity disorder (ADHD) relative to the rest of the population, and to examine the predictive value of the SDQ for outcome of parent-reported clinical diagnosis of ASD/ADHD. A secondary aim was to examine the extent of overlap in symptoms between children diagnosed with these two disorders, as measured by the SDQ subscales. A cross-sectional secondary analysis of data from the Millennium Birth Cohort (n=19,519), was conducted. Data were weighted to be representative of the UK population as a whole. ADHD or ASD identified by a medical doctor or health professional were reported by parents in 2008 and this was the case definition of diagnosis; (ADHD n=173, ASD n=209, excluding twins and triplets). Study children's ages ranged from 6.3-8.2 years; (mean 7.2 years). Logistic regression was used to examine the association between the parent-reported clinical diagnosis of ASD/ADHD and teacher and parent-reported SDQ subscales. All SDQ subscales were strongly associated with both ASD and ADHD. There was substantial co-occurrence of behavioral difficulties between children diagnosed with ASD and those diagnosed with ADHD. After adjustment for other subscales, the final model for ADHD, contained hyperactivity/inattention and impact symptoms only and had a sensitivity of 91% and specificity of 90%; (AUC) =0.94 (95% CI, 0.90-0.97). The final model for ASD was composed of all subscales except the 'peer problems' scales, indicating of the complexity of behavioural difficulties that may accompany ASD. A threshold of 0.03 produced model sensitivity and specificity of 79% and 93% respectively; AUC=0.90 (95% CI, 0.86-0.95). The results support changes to DSM-5 removing exclusivity clauses.

A MULTIVARIATE SURFACE-BASED ANALYSIS OF THE PUTAMEN IN PREMATURE NEWBORNS: REGIONAL DIFFERENCES WITHIN THE VENTRAL STRIATUM.


Many children born preterm exhibit frontal executive dysfunction, behavioral problems including attentional deficit/hyperactivity disorder and attention related learning disabilities. Anomalies in regional specificity of cortico-striato-thalamo-cortical circuits may underlie deficits in these disorders. Nonspecific volumetric deficits of striatal structures have been documented in these subjects, but little is known about surface deformation in these structures. For the first time, here we found regional surface morphological differences in the preterm neonatal ventral striatum. We performed regional group comparisons of the surface anatomy of the striatum (putamen and globus pallidus) between 17 preterm and 19 term-born neonates at term-equivalent age. We reconstructed striatal surfaces from manually segmented brain magnetic resonance images and analyzed them using our in-house conformal mapping program. All surfaces were registered to a template with a new surface fluid registration method. Vertex-based statistical comparisons between the two groups were performed via four methods: univariate and multivariate tensor-based morphometry, the commonly used medial axis distance, and a combination of the last two statistics. We found statistically significant differences in regional morphology between the two groups that are consistent across statistics, but more extensive for multivariate measures. Differences were localized to the ventral aspect of the striatum. In particular, we found abnormalities in the preterm anterior/inferior putamen, which is interconnected with the medial orbital/prefrontal cortex and the midline thalamic nuclei including the medial dorsal nucleus and pulvinar. These findings support the hypothesis that the ventral striatum is vulnerable, within the cortico-stiato-thalamo-cortical neural circuitry, which may underlie the risk for long-term development of frontal executive dysfunction, attention deficit hyperactivity disorder and attention-related learning disabilities in preterm neonates.
THE IMPACT OF FINANCIAL REWARD CONTINGENCIES ON COGNITIVE FUNCTION PROFILES IN ADULT ADHD.

**OBJECTIVES:** Although it is well established that cognitive performance in children with attention-deficit/hyperactivity disorder (ADHD) is affected by reward and that key deficits associated with the disorder may thereby be attenuated or even compensated, this phenomenon in adults with ADHD has thus far not been addressed. Therefore, the aim of the present study was to examine the motivating effect of financial reward on task performance in adults with ADHD by focusing on the domains of executive functioning, attention, time perception, and delay aversion.

**METHODS:** We examined male and female adults aged 18-40 years with ADHD (n = 38) along with a matched control group (n = 40) using six well-established experimental paradigms.

**RESULTS:** Impaired performance in the ADHD group was observed for stop-signal omission errors, n-back accuracy, reaction time variability in the continuous performance task, and time reproduction accuracy, and reward normalized time reproduction accuracy. Furthermore, when rewarded, subjects with ADHD exhibited longer reaction times and fewer false positives in the continuous performance task, which suggests the use of strategies to prevent impulsivity errors.

**CONCLUSIONS:** Taken together, our results support the existence of both cognitive and motivational mechanisms for the disorder, which is in line with current models of ADHD. Furthermore, our data suggest cognitive strategies of “stopping and thinking” as a possible underlying mechanism for task improvement that seems to be mediated by reward, which highlights the importance of the interaction between motivation and cognition in adult ADHD.

MODERATORS OF TREATMENT RESPONSE IN ADULTS WITH ADHD TREATED WITH A VITAMIN-MINERAL SUPPLEMENT.

**Background:** To date there has been no research investigating moderators of response to micronutrient treatment of mental illness, specifically baseline nutrient levels.

**Method:** We conducted analyses of data from a randomized placebo-controlled trial (RCT) of 80 adults ((greater-than or equal to). 16. years) with Attention-Deficit/Hyperactivity Disorder (ADHD), whereby participants were treated acutely (8. weeks) with micronutrients or placebo followed by an open-label (OL) phase of 8. weeks whereby all participants received micronutrients. To ensure that all participants had been exposed to the micronutrients for 8. weeks, only those 64 who had adhered to the treatment protocol and completed 8. weeks on nutrients were included in the data analysis: 34 from the group that had been randomized to the micronutrient arm, and 30 from the group that had been randomized to the placebo group and hence had only received nutrients in the OL phase. Six outcomes were examined: change in ADHD symptoms (self/clinician), ADHD responder, Clinical Global Impression-Improvement (CGI-I), change in mood, and change in Global Assessment of Functioning (GAF). Demographic, developmental and psychiatric history, current clinical characteristics, and baseline nutrient levels were all considered as putative predictors.

**Results:** There were significant changes in all outcome variables after 8weeks exposure to the micronutrients. Among the nutrients recorded at baseline, substantial deficiencies (27%) were only observed for vitamin D. However, other than an association showing that higher iron at baseline was correlated with higher baseline depression scores, baseline nutrient levels were not correlated with baseline psychiatric variables/current clinical characteristics. Regression analyses revealed that higher baseline ferritin and lower baseline copper and vitamin D levels were associated with a better response to treatment for some but not all outcomes. None of the other nutrient levels was found to be associated with outcome, including zinc, vitamin B12, iron, and folate. There were no childhood risk factors, demographic variables or clinical correlates that contraindicated micronutrient treatment; more severe symptoms at baseline and greater number of developmental risk factors predicted greater treatment response.
Conclusions: Further research looking at nutrients more broadly is required to confirm these initial observations about ferritin, vitamin D and copper; however, the results suggest that serum nutrient levels have limited value for identifying who will respond to treatment.

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**DISCONTINUOUS COLLEGE ENROLLMENT: ASSOCIATIONS WITH SUBSTANCE USE AND MENTAL HEALTH.**

**Arria AM, Caldeira KM, Vincent KB, et al.**

**OBJECTIVE:** This study examined the prospective relationship of substance use and mental health problems with risk of discontinuous enrollment in college.

**METHODS:** Participants were 1,145 students at a large public university who were interviewed annually for four years beginning at college entry in 2004 (year 1). Discontinuous enrollment was defined as a gap in enrollment of one or more semesters during the first two years (early discontinuity) or the second two years (late discontinuity) versus continuous enrollment throughout all four years. Explanatory variables measured in year 1 were scores on the Beck Depression Inventory (BDI) and the Beck Anxiety Inventory, childhood conduct problems, cannabis use, number of illicit drugs used, and alcohol consumption. In years 3 and 4, participants reported lifetime history of clinically diagnosed attention-deficit hyperactivity disorder, depression, and anxiety, including age at diagnosis. Multinomial logistic regression models were developed to evaluate the association between the independent variables and discontinuous enrollment while holding constant background characteristics.

**RESULTS:** Higher BDI scores predicted early discontinuity but not late discontinuity, whereas cannabis and alcohol use predicted only late discontinuity. Receiving a depression diagnosis during college was associated with both early and late discontinuity. Self-reported precollege diagnoses were not related to discontinuous enrollment once background characteristics were taken into account.

**CONCLUSIONS:** Students who experience depressive symptoms or seek treatment for depression during college might be at risk of interruptions in their college enrollment. Cannabis use and heavy drinking appear to add to this risk. Students entering college with preexisting psychiatric diagnoses are not necessarily at risk of enrollment interruptions.


**PREVALENCE AND PATTERNS OF PSYCHIATRIC DISORDERS IN REFERRED ADOLESCENTS WITH INTERNET ADDICTION.**

**Bozkurt H, Coskun M, Ayaydin H, et al.**

**AIM:** To investigate prevalence and patterns of psychiatric disorders in young subjects with Internet addiction (IA).

**METHODS:** Subjects were taken from a sample of patients, aged 10-18 years old, referred to Istanbul Medical Faculty, Child and Adolescent Psychiatry Department due to a variety of behavioral and emotional problems alongside problematic Internet use. Inclusion criteria included IQ >/=70 and score >/=80 on Young’s Internet Addiction Scale (YIAS). Psychiatric comorbidity was assessed using the Turkish version of the Schedule for Affective Disorders and Schizophrenia for School Age Children-Present and Lifetime Version.

**RESULTS:** Subjects were 45 boys (75%) and 15 girls (25%) with an age range of 10-18 years old (mean age, 13.38 +/- 1.79 years). A total of 60% (n=36) had been using Internet for >/=5 years. Mean hours/week spent on the Internet was 53.7 (range, 30-105 h) and the average YIAS score was 85. All subjects (100%) had at least one and 88.3% (n = 53) had at least two comorbid psychiatric disorders. The frequency of diagnostic groups were as follows: behavioral disorder, n=52 (86.7%); anxiety disorder, n=43 (71.7%); mood disorder, n=23 (38.3%); elimination disorder, n=16 (26.7%); tic disorder, n=10 (16.7%); and substance use disorder, n=4 (6.7%). The most common psychiatric disorders were attention-deficit hyperactivity disorder (n=53; 83.3%), social phobia (n=21; 35.0%) and major depressive disorder (n=18; 30.0%).

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CONCLUSION: High rates of psychiatric comorbidity, particularly behavioral, anxiety and mood disorders were found in young subjects with IA. Because the presence of psychiatric disorders may affect the management/prognosis of IA, assessment should include that for other psychiatric disorders.

Validity of Conners' Adult Attention-Deficit/Hyperactivity Disorder Rating Scale-Investigator Rated: Screening Version in Patients from Within and Outside of Europe.

Sandra Kooij JJ, Keith CC, Goto T, et al.

In adult patients with attention-deficit/hyperactivity disorder from within and outside of Europe, Conners' Adult Attention-Deficit/Hyperactivity Disorder (ADHD) Rating Scale-Investigator Rated: Screening Version showed good internal consistency (Cronbach's alpha=0.930 and 0.938, respectively) and convergent validity with the Clinical (Pearson's correlation coefficients: 0.65-0.82, P<0.001) Global Impression-ADHD-Severity scale over 12 weeks of pharmacological treatment.

Association Between SYP with Attention-Deficit/Hyperactivity Disorder in Chinese Han Subjects: Differences Among Subtypes and Genders.


Dysfunction of neurotransmitters has been suggested to be involved in the etiology of attention-deficit/hyperactivity disorder (ADHD). Hence, genes encoding proteins involved in the vesicular release process of those neurotransmitters are attractive candidates in ADHD genetics. One of these genes is SYP, which encodes synaptophysin, a protein known to participate in regulating neurotransmitter release and synaptic plasticity. Several studies have reported an association between SYP and ADHD, but more work is needed to refine the association. In the present study, we attempt to investigate their association in Chinese Han subjects by family-based and case-control studies. Transmission disequilibrium tests (TDTs) in 1112 trios found significant association between SYP and the predominantly inattentive subtype (ADHD-I), especially for males with ADHD-I, both from single nucleotide polymorphism (SNP) and haplotypic analyses. Chi-square tests in 1682 ADHD probands and 957 comparison subjects indicated possible association of SYP with female ADHD and female ADHD-I. However, the associated alleles and haplotypes between males and females were reversed. In conclusion, our results suggested that SYP may be primarily associated with ADHD-I and its genetic mechanism may be gender-specific. Thus, it is necessary to take subtype and gender into account in ADHD genetic studies.

Attentional WM is Not Necessarily Specifically Related with Fluid Intelligence: The Case of Smart Children with ADHD Symptoms.


Executive functions and, in particular, Attentional (active) Working Memory (WM) have been associated with fluid intelligence. The association contrasts with the hypothesis that children with ADHD exhibit problems with WM tasks requiring controlled attention and may have a good fluid intelligence. This paper examines whether children who are intelligent but present ADHD symptoms fail in attentional WM tasks. The latter result would be problematic for theories assuming the generality of a strict relationship between intelligence and WM. To study these issues, a battery of tests was administered to a group of 58 children who all displayed symptoms of ADHD. All children were between the age of 8 and 11 years, and were described by their teachers as smart. Children were compared to a control group matched for age, schooling, and gender. The battery included a test of fluid intelligence (Raven's Coloured Matrices), and a series of visuospatial WM tasks. Results showed that children with ADHD were high in intelligence but significantly lower than the controls in WM tasks requiring high attentional control, whereas there was no
difference in WM tasks requiring low attentional control. Furthermore, only high attentional control WM tasks were significantly related to Raven's performance in the control group, whereas all WM tasks were similarly related in the ADHD group. It is concluded that performance in high attentional control WM tasks may be related to fluid intelligence, but also to a specific control component that is independent of intelligence and is poor in children with ADHD.


EFFECTS OF SMOKING ABSTINENCE ON SMOKING-REINFORCED RESPONDING, WITHDRAWAL, AND COGNITION IN ADULTS WITH AND WITHOUT ATTENTION DEFICIT HYPERACTIVITY DISORDER.

Kollins SH, English JS, Roley ME, et al.

RATIONALE: Individuals with attention deficit hyperactivity disorder (ADHD) have a more difficult time quitting smoking compared to their non-ADHD peers. Little is known about the underlying behavioral mechanisms associated with this increased risk.

OBJECTIVES: This study aims to assess the effects of 24-h smoking abstinence in adult smokers with and without ADHD on the following outcomes: smoking-reinforced responding, withdrawal, and cognitive function.

METHODS: Thirty-three (n=16 with ADHD, 17 without ADHD) adult smokers (more than or equal to ten cigarettes/day) were enrolled. Each participant completed two experimental sessions: one following smoking as usual and one following biochemically verified 24-h smoking abstinence. Smoking-reinforced responding measured via a progressive ratio task, smoking withdrawal measured via questionnaire, and cognition measured via a continuous performance test (CPT) were assessed at each session.

RESULTS: Smoking abstinence robustly increased responding for cigarette puffs in both groups, and ADHD smokers responded more for puffs regardless of condition. Males in both groups worked more for cigarette puffs and made more commission errors on the CPT than females, regardless of condition. Smoking abstinence also increased ratings of withdrawal symptoms in both groups and smokers with ADHD, regardless of condition, reported greater symptoms of arousal, habit withdrawal, and somatic complaints. Across groups, smoking abstinence decreased inhibitory control and increased reaction time variability on the CPT. Abstinence-induced changes in inhibitory control and negative affect significantly predicted smoking-reinforced responding across groups.

CONCLUSIONS: Smokers with ADHD reported higher levels of withdrawal symptoms and worked more for cigarette puffs, regardless of condition, which could help explain higher levels of nicotine dependence and poorer cessation outcomes in this population. Abstinence-induced changes in smoking-reinforced responding are associated with changes in inhibitory control and negative affect regardless of ADHD status, a finding that may lead to novel prevention and treatment programs.

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STRUCTURED DYADIC BEHAVIOR THERAPY PROCESSES FOR ADHD INTERVENTION.

Curtis DF.

Children with Attention-Deficit/Hyperactivity Disorder (ADHD) present significant problems with behavioral disinhibition that often negatively affect their peer relationships. Although behavior therapies for ADHD have traditionally aimed to help parents and teachers better manage children's ADHD-related behaviors, therapy processes seldom use peer relationships to implement evidence-based behavioral principles. This article introduces Structured Dyadic Behavior Therapy as a milieu for introducing effective behavioral techniques within a socially meaningful context. Establishing collaborative behavioral goals, benchmarking, and redirection strategies are discussed to highlight how in-session dyadic processes can be used to promote more meaningful reinforcement and change for children with ADHD. Implications for improving patient care, access to care, and therapist training are also discussed.
Health, chronic conditions, and behavioral risk disparities among U.S. immigrant children and adolescents.

Singh GK, Yu SM, Kogan MD.

Objective: We examined differentials in the prevalence of 23 parent-reported health, chronic condition, and behavioral indicators among 91,532 children of immigrant and U.S.-born parents.

Methods: We used the 2007 National Survey of Children's Health to estimate health differentials among 10 ethnic-nativity groups. Logistic regression yielded adjusted differentials.

Results: Immigrant children in each racial/ethnic group had a lower prevalence of depression and behavioral problems than native-born children. The prevalence of autism varied from 0.3% among immigrant Asian children to 1.3%-1.4% among native-born non-Hispanic white and Hispanic children. Immigrant children had a lower prevalence of asthma, attention deficit disorder/attention deficit hyperactivity disorder; developmental delay; learning disability; speech, hearing, and sleep problems; school absence; and >/= 1 chronic condition than native-born children, with health risks increasing markedly in relation to mother's duration of residence in the U.S. Immigrant children had a substantially lower exposure to environmental tobacco smoke, with the odds of exposure being 60%-95% lower among immigrant non-Hispanic black, Asian, and Hispanic children compared with native non-Hispanic white children. Obesity prevalence ranged from 7.7% for native-born Asian children to 24.9%-25.1% for immigrant Hispanic and native-born non-Hispanic black children. Immigrant children had higher physical inactivity levels than native-born children; however, inactivity rates declined with each successive generation of immigrants. Immigrant Hispanic children were at increased risk of obesity and sedentary behaviors. Ethnic-nativity differentials in health and behavioral indicators remained marked after covariate adjustment.


ADHD among adolescents with intellectual disabilities: pre-pathway influences.

Neece CL, Baker BL, Lee SS.

Children and adolescents with intellectual disabilities (ID) are at heightened risk for developing ADHD. However, the validity of ADHD as a diagnosis for youth with ID remains controversial. To advance research on validity, the present study examined the hypothesized precursors to ADHD in typically developing adolescents (TD) and adolescents with ID, specifically with regard to family history of ADHD, molecular genetics, and neuropsychological functioning. Results indicated that youth ADHD symptoms were related to parental ADHD symptoms regardless of the adolescent’s cognitive functioning. Additionally, findings suggested that the DRD4 genetic variant and adolescent set-shifting abilities were related to adolescent ADHD symptoms independent of the adolescent’s cognitive functioning. This study provides an initial investigation of the biological correlates of ADHD among youth with ID.

The effect of different stimulus attributes on the attentional performance of children with attention deficit/hyperactivity disorder and dyslexia.

Wang LC, Tsai HJ, Yang HM.

While teachers have traditionally used the interesting objects to increase student attention in the classroom, evidence supporting the effectiveness of this method is lacking. The present study investigated the influence of different stimulus attributes for typical developing students and for students with attention deficit/hyperactivity disorder (ADHD) and dyslexia. Thirty children with ADHD, 30 children with dyslexia, and 30 typical developing students were tested using a measuring tool that was constructed by the authors to assess their sustained attention and selective attention on the geometric-figure assessment and the
interesting-figure assessment. The geometric-figure assessment included a square, circle, trapezium, and triangle; and the interesting-figure assessment included a house, cat, hand, and tree. While the typical developing group showed better selective attention on the geometric-figure assessment, there was no difference between the dyslexic group and the ADHD group with respect to selective attention. Furthermore, the typical developing and dyslexic groups did not differ in the geometric-figure assessment in sustained attention and were both better in this area than the ADHD group. In the interesting-figure assessment, the typical developing and dyslexic groups performed similarly in sustained attention, but selective attention of the dyslexic group improved more than the ADHD group, similar to the typical developing group. Both selective attention of the dyslexic group and sustained attention of the ADHD group showed positive significant differences in the interesting-figure assessment, but sustained attention of the dyslexic group and selective attention of the ADHD group showed little difference in the interesting-figure assessment. Surprisingly, the typical developing group did not show any significant difference in the interesting-figure assessment, possibly because they had previously demonstrated a ceiling effect in the geometric-figure assessment.


DEVELOPMENTS AND CHALLENGES IN THE DIAGNOSIS AND TREATMENT OF ADHD.
Attention-deficit/hyperactivity disorder (ADHD) is a prevalent neurodevelopmental disorder, often associated with other psychiatric comorbidities, functional impairments, and poor long-term outcomes. The objective of this selected review is to describe current advances and challenges in the diagnosis and treatment of ADHD. The disorder is associated with neurobiological underpinnings and is highly heterogeneous in various aspects, such as symptom profiles, cognitive impairments, and neurobiological and genetic features. The efficacy and safety of short-term pharmacological treatments across the life cycle is well studied, but further research investigating long-term treatment, impact of treatment in preschoolers, and non-pharmacological interventions is needed. Future research is also needed to better characterize the neurodevelopmental pathways of the disorder, linking clinical and neurobiological information, less investigated populations, and new interventions.

SCREENING FOR ATTENTION DEFICIT HYPERACTIVITY DISORDER IN ADULT PATIENTS IN PRIMARY CARE.
Aragones E, Canisa A, Caballero A, et al.
AIMS. To estimate the proportion of adult patients in primary care with a positive screening test for attention deficit hyper-activity disorder (ADHD) and to analyse their characteristics.

PATIENTS AND METHODS. A cross-sectional descriptive study was performed in nine primary care clinics in the province of Tarragona. The sample consisted of 432 consecutive patients in primary care who visited for any reason, with ages ranging from 18 to 55 years. Screening for ADHD was carried out by means of the Adult ADHD Self-Report Scale (ASRS). Data about functional impact (Sheehan Disability Inventory) were obtained and a review of the patient records provided data concerning psychiatric comorbidity and the consumption of psychopharmaceuticals.

RESULTS. The percentage of positive results in the screening tests was 19.9% (95% CI = 16.4-23.9%). Taking into account the sensitivity and specificity of the ASRS, the 'real' prevalence was estimated to be 12.5% (95% CI = 8.2-16.8%). None of these patients were diagnosed or treated for ADHD. Positive screening tests are associated with occupational, social and familial dysfunction, and greater perceived stress. There is also a higher level of comorbidity with affective disorders and substance abuse, as well as greater use of psychopharmaceuticals.

CONCLUSIONS. Screening for ADHD in adult patients in primary care gives rise to a notably high proportion of positive screening test results, which suggests that there could be a significant prevalence of patients with ADHD. These data contrast with the absence of this diagnosis in the patient records. Further
research is needed to determine the usefulness of the diagnosis of ADHD and the possible role that must be played by primary care.

Schizophr Res. 2013 Jul;147:301-09.
**FAILURE OF ATTENTION FOCUS AND COGNITIVE CONTROL IN SCHIZOPHRENIA PATIENTS WITH AUDITORY VERBAL HALLUCINATIONS: EVIDENCE FROM DICHOTIC LISTENING.**
Auditory verbal hallucinations (AVHs) are speech perceptions that lack an external source, phenomenologically experienced as "hearing voices". A perceptual origin of an AVH experience in patients with schizophrenia can however not explain why the "voices" drain the attentional and cognitive capacity of the patients, making them unable to direct attention away from the "voices" and to cognitively suppress the experience. We recently reported how AVHs interfere with the perception of speech sounds, using a dichotic listening experimental paradigm. We now extend this finding by reporting on the interference caused by AVHs on attention and cognitive control, using a slight variation of the same dichotic listening paradigm. The patients (N=148) were instructed to pay attention to and report from either the right or left ear syllable of the dichotic pair. We then correlated their PANSS score for the hallucination item (P3) with the performance score on the dichotic listening task. The results showed that AVHs interfered with the ability to report the right ear syllable when instructed to pay attention to the right side, which is a marker of inability to attend to an external speech stimulus. When instructed to pay attention to the left side, AVHs interfered with the ability to report the left ear syllable, which is a marker of inability to use cognitive control to suppress attending to the "voices". The corresponding correlations for the emotional withdrawal (N2) negative symptom were all non-significant. The correlations were substantiated in an ANOVA with corresponding significant group differences between high versus low symptom score groups. The results thus extend our previous findings of a perceptual origination for AVHs by showing that AVHs interfere with the ability to attend to the outer world around the patient, and the ability to inhibit, or suppress, the "voices" once they occur. Future research should pin down the neuronal basis of both the origination and the attentional and cognitive control aspects of AVHs.

School Mental Health. 2013 Dec;5:175-82.
**RACIAL DIFFERENCES IN MEDICATION USE IN A NATIONAL SAMPLE OF CHILDREN WITH ADHD ENROLLED IN SPECIAL EDUCATION.**
Graves SLJ, Serpell Z.
The purpose of this study was to examine the extent of medication use among elementary school students in special education diagnosed with attention deficit hyperactivity disorder (ADHD). In addition, researchers sought to understand whether the frequency of medication use varied by demographic factors such as ethnic group and age. Participants were children enrolled in the nationally representative Special Education Elementary Longitudinal Study. Results indicate that significant discrepancies exist between African–American children and their other-race counterparts in ADHD medication use. Additionally, younger children were more likely to take medication than older children, and the higher the parents’ educational level, the more likely their children took medication. Implications for ADHD treatment among racially diverse populations are discussed.

**SIBSHIP SIZE, BIRTH ORDER, FAMILY STRUCTURE AND CHILDHOOD MENTAL DISORDERS.**
PURPOSE: The aim of this study was to determine the role that birth order, sibship size and family structure have as risk factors in the development of common childhood mental disorders.
METHOD: A case-control study design was conducted (N=16,823). The group under study consisted of all those subjects who had consulted with a psychiatrist/psychologist and had received a clinical diagnosis at public mental health centres within the Region of Madrid (Spain), between 1980 and 2008. A multiple logistic regression was used to explore the independent association with each diagnosis: emotional disorders (ED) with onset specific to childhood, attention deficit hyperactivity disorder (ADHD), conduct disorder (CD), mental retardation (MR), and pervasive developmental disorder (PDD).

RESULTS: Birth order and family structure significantly predicted the risk of being diagnosed with ED or ADHD. In addition, sibship size and sex predicted the risk of being diagnosed with a childhood mental disorder.

CONCLUSIONS: We concluded that being the middle child and living with both biological parents appear to be protective factors against the development of ED or ADHD. Living in large families appears to increase the risk of receiving a CD, MR, or PDD diagnosis. Further research is warranted.

A STUDY ON THE EFFECTIVENESS OF VIDEOCONFERENCING ON TEACHING PARENT TRAINING SKILLS TO PARENTS OF CHILDREN WITH ADHD.
Xie Y, Dixon JF, Yee OM, et al.

OBJECTIVE: Many geographic locations are without services and staff available to provide treatment for children with attention deficit hyperactivity disorder (ADHD). This is a randomized controlled trial to evaluate the effectiveness of group parent training on ADHD treatment delivered via videoconferencing.

SUBJECTS AND METHODS: Twenty-two subjects were enrolled in the study, with 9 subjects in the videoconference session (treatment group) and 13 in the face-to-face session (control group). The parent-child relationship questionnaire for child and adolescents (PCQ-CA), Vanderbilt assessment scales (parent and teacher versions), children global assessment scale, clinical global impression-severity score, clinical global impression-improvement score, and social skills rating system assessed the effectiveness of the treatment. A Likert scale evaluated parents' acceptance of the training modality. Our results showed that the parent training program significantly improved parents' disciplinary practices based on the PRQ-CA, parent ratings of ADHD, oppositional defiant disorder, and conduct disorder symptoms, and the children's global functioning.

RESULTS: The treatment effects did not differ between the videoconference and face-to-face groups; however, the videoconference group evidenced statistically greater improvement on the hyperactive symptoms of Vanderbilt assessment scales. Our findings suggest that parent training through a videoconferencing modality may be as effective as face-to-face training and is well accepted by parents.

CONCLUSIONS: Parent training via videoconferencing may be an important tool for addressing ADHD in geographic locations that do not have access to appropriate treatment providers.

EFFECTS OF METHYLPHENIDATE ON ACTUTE MATH PERFORMANCE IN CHILDREN WITH ATTENTION-DEFICIT HYPERACTIVITY DISORDER.
Grizenko N, Cai E, Jolicoeur C, et al.

Objective: Examine the short-term (acute) effects of methylphenidate (MPH) on math performance in children with attention-deficit hyperactivity disorder (ADHD) and what factors predict improvement in math performance.

Method: One hundred ninety-eight children with ADHD participated in a double-blind, placebo-controlled, randomized crossover MPH trial. Math response to MPH was determined through administration of math problems adjusted to their academic level during the Restricted Academic Situation Scale (RASS). Student t tests were conducted to assess change in math performance with psychostimulants. Correlation between change on the RASS and change on the math performance was also examined. Linear regression was performed to determine predictor variables.
**Results:** Children with ADHD improved significantly in their math with MPH (P < 0.001). The degree of improvement on the RASS (which evaluates motor activity and orientation to task) and on math performance on MPH was highly correlated. A child's age at baseline and Wechsler Individual Achievement Test (WIAT)-Numerical Operations standard scores at baseline accounted for 15% of variances for acute math improvement.

**Conclusions:** MPH improves acute math performance in children with ADHD. Younger children with lower math scores (as assessed by the WIAT) improved most on math scores when given psychostimulants.


**INDIVIDUALS EXHIBIT IDIOSYNCRATIC EYE-MOVEMENT BEHAVIOR PROFILES ACROSS TASKS.**

**Poynter W, Barber M, Inman J, et al.**

The purpose of this study was to examine individual differences in eye-movement behavior. Six metrics (Fixation Rate, Duration, and Size; Saccade Amplitude; Micro-Saccade Rate and Amplitude) were used to measure individuals' eye-movement behavior profiles (EmBP). We replicate previous research (Andrews & Coppola, 1999; Castelhano & Henderson, 2008) by finding consistent individual differences in fixation duration and saccade amplitude across tasks, and present new findings of stable idiosyncrasies in measures of fixational eye-movement (Fixation Size, Micro-Saccade Rate and Amplitude). Moreover, we observed consistent inter-metric correlations across tasks (e.g., individuals that exhibited relatively high Fixation Rates also presented relative low Micro-Saccade Rates and relatively high Micro-Saccade Amplitudes). Factor Analysis linked the six EmBP metrics together with a single factor, which we speculate might be related to the operational effectiveness of the attentional system, given that individual factor scores were correlated with scores on a self-report measure of attentional function. Normal subjects with relatively high scores on this attention-deficit measure exhibited relatively frequent fixations of short duration and large spatial extent, and relatively infrequent micro-saccades of large amplitude. This EmBP is similar to a general pattern of eye-movement behavior observed with ADHD individuals - difficulty controlling eye movements, maintaining fixation, and inhibiting intrusive saccades. Results of this study indicate that normal individuals exhibit idiosyncratic EmBPs that are quite stable across tasks and are related to attentional ability.


**IS ADHD A RISK FOR POSTTRAUMATIC STRESS DISORDER (PTSD)? RESULTS FROM A LARGE LONGITUDINAL STUDY OF REFERRED CHILDREN WITH AND WITHOUT ADHD.**

**Biederman J, Petty C, Spencer TJ, et al.**

**Objectives.** Preclinical studies link prenatal nicotine exposure with the development of both ADHD-like phenotype in rodents and blockade of extinction learning in a fear conditioning paradigm, a preclinical model of posttraumatic stress disorder (PTSD). While these findings suggest that either ADHD, prenatal nicotine exposure, or both could be a risk factor for PTSD, such associations have not been investigated in humans.

**Methods.** Subjects were ascertained from family-genetic, longitudinal studies of paediatrically and psychiatrically referred children with and without ADHD of both sexes and their siblings followed for 10 years from childhood into adulthood (n=403 probands; n=464 siblings; mean age at follow-up of probands and siblings=22.0 years). All subjects were comprehensively evaluated with structured diagnostic interviews that included questions regarding prenatal use of cigarettes.

**Results.** A total of 12% (104/867) of the sample had been exposed to maternal smoking during pregnancy. There was no interaction effect between maternal smoking during pregnancy and ADHD (z=0.01, P=0.99). Maternal smoking during pregnancy and ADHD were independent, significant risk factors for PTSD at the 10-year follow-up (odds ratio=3.58 [1.35,9.48], z=2.57, P=0.01 and odds ratio=2.23 [1.06,4.69], z=2.11, P = 0.04, respectively).
Conclusions. These results suggest that both maternal smoking during pregnancy and ADHD are significant predictors of PTSD in humans.


AUTONOMIC HYPOACTIVITY IN BOYS WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER AND THE INFLUENCE OF METHYLPHENIDATE.
Conzelmann A, Gerdes ABM, Mucha RF, et al.

Objectives. This study investigates an overall autonomic hypoactivity reflecting hypoarousal as important aetiological factor in ADHD at baseline during rest and in response towards stimuli. In addition, effects of methylphenidate (MPH) are examined. We further assessed whether this hypoarousal is a stable characteristic or ameliorated by arousing emotional stimuli.

Methods. Boys with ADHD were examined with (n = 35) or without MPH (n=45) and compared with healthy boys (n=22) regarding skin conductance level (SCL) during rest and skin conductance responses (SCRs) as well as valence and arousal ratings in response to positive, neutral, and negative pictures.

Results. ADHD children without MPH were characterized by reduced baseline SCL and overall reduced SCRs. ADHD children with MPH never differed from control children. All groups displayed normal valence and arousal ratings of the stimuli and enhanced SCRs to emotional in comparison to neutral pictures.

Conclusions. This is the first study to unravel (1) a general autonomic hypoactivity in ADHD children at baseline and in response to low arousing neutral and highly arousing emotional stimuli, and (2) hints that MPH normalizes this hypoactivity. Results contribute to the understanding of ADHD aetiology and MPH functionality, and are consistent with the cognitive-energetic model of ADHD.


WHAT HAPPENS TO CHILDREN AND ADOLESCENTS WITH MENTAL DISORDERS? FINDINGS FROM LONG-TERM OUTCOME RESEARCH.
Steinhausen HC.

Research on the long-term outcome of mental disorders originating in childhood and adolescence is an important part of developmental psychopathology. After a brief sketch of relevant terms of outcome research, the first part of this review reports findings based on heterotypic cohort studies. The major second part of this review presents findings based on long-term outcome studies dealing with homotypic diagnostic groups. In particular, the review focuses on the course and prognosis of ADHD, anxiety disorders, depression, conduct disorders, eating disorders, autism spectrum disorders, schizophrenia, and selective mutism. Findings mainly support the vulnerability hypothesis regarding mental disorders with early manifestation in childhood and adolescence as frequent precursors of mental disorders in adulthood. The discussion focuses on the impact of early manifesting disorders in the frame of general mental morbidity and of the effect of interventions, which is not yet sufficiently discernible.
AUTISMO
UN’UMANITA’ POSSIBILE

Prof. Francesco BARALE

Esperienza di Cascina Rossago RSD

Mercoledì, 5 marzo 2014
ore 14,00 - aula Guasti

IRCCS Istituto di Ricerche Farmacologiche Mario Negri
Via G. La Masa, 19 - 20156 Milano

Save the date
I disturbi dell’apprendimento in una società disattenta
Prof. Cristiano TERMINE

Mercoledì, 16 aprile 2014
ore 14,00 - aula Guasti

IRCCS Istituto di Ricerche Farmacologiche Mario Negri
Via G. La Masa, 19 - 20156 Milano

Save the date
Iniziativa nell’ambito del Progetto di Neuropsichiatria dell’Infanzia e dell’Adolescenza
Il Progetto è realizzato con il contributo, parziale, della Regione Lombardia
(in attuazione della D.G. sanità n. 3250 del 11/04/2011)
Capofila Progetto: UONPIA Azienda Ospedaliera “Spedali Civili di Brescia”
“Condivisione dei percorsi diagnostico-terapeutici per l’ADHD in Lombardia”. 

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