NEWSLETTER

INDICE:

ISTITUTO DI RICERCHE FARMACOLOGICHE MARIO NEGRI IRCCS

BIBLIOGRAFIA ADHD MARZO 2017

Acta Medica Mediterranea. 2016;32:1756-59.

ADHD-LIKE SYMPTOMS IN CHILDREN AFFECTED BY OBSTRUCTIVE SLEEP APNEA SYNDROME: A CASE-CONTROL STUDY.

Precenzano F, Ruberto M, Parisi L, et al.

Introduction: ADHD is characterized by inattention, hyperactivity, impulsivity, or a combination of these symptoms. Sleep disorders may be considered as a not secondary underlying cause of ADHD and growing evidence evidenced that obstructive sleep apnea syndrome (OSA) symptoms may overlap ADHD's ones. Aim of the present study is verifying the presence of ADHD-like symptoms in other frequent condition such as sleep-related breathing disorders in pediatric age.

Materials and methods: 34 children (19 males and 15 females) aged 6-10 years (mean age 9.706 ± 3.434) with polysomnographic diagnosis of OSA, according to ICSD-3 criteria, were recruited. Control group was composed by 89 typical developing children (47 males, 42 females) (mean age 9,528 ± 3,351). The Conners' Rating Scale- Revised (CRS-R) test was administered to mothers to assess their children's behavior.

Results: The two groups are comparable for age (p = 0.794) and sex distribution (p = 0.918). Subjects affected by OSA present higher scores in pathological range in all scales of CRS-R than controls (Table 1).

Conclusions: Scientific and clinical evidences tend to stress the similarities between ADHD and OSA effects/comorbidities in pediatric age, suggesting sleep screening as mandatory before starting stimulant drugs treatment

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Per la ricerca degli articoli pubblicati nella letteratura scientifica nel mese in esame sono state consultate le banche dati Medline, Embase, PsycINFO e PsycArticle utilizzando le seguenti parole chiave (o i loro sinonimi): 'Attention deficit disorder', 'Attention deficit hyperactivity disorder', 'Infant', 'Child', 'Adolescent', 'Human'. Sono qui riportate le referenze considerate rilevanti e pertinenti.

Acta Paediatr. 2017 Jan;106:87-94.

ANTIBIOTICS IN THE FIRST YEAR OF LIFE AND SUBSEQUENT NEUROCOGNITIVE OUTCOMES.

Slykerman RF, Thompson J, Waldie KE, et al.

AIM: There may be a link between disruption to the gut microbiota in early life and later neurocognitive outcomes. We hypothesised that antibiotic use in early life is associated with a detrimental effect on later neurocognitive outcomes.

METHODS: Eight hundred and seventy-one European mothers and their children enrolled in the Auckland Birthweight Collaborative Study at birth. Information on antibiotic use during the first year of life and between 12 months and three-and-a-half years of age was gathered via maternal interview. Intelligence test scores and measures of behavioural difficulties were obtained when children were three-and-a-half years, seven years and 11 years of age.

RESULTS: Antibiotic use in the first year of life was reported in 70% of the 526 children with antibiotic data assessed at age three-and-a-half years. Those who had received antibiotics had more behavioural difficulties and more symptoms of depression at follow-up. Results were consistent across all standardised psychologist administered tests, as well as parent rated, teacher rated and self-report measures.

CONCLUSION: This study demonstrates an association between antibiotic use in the first year of life and subsequent neurocognitive outcomes in childhood. If confirmed by further research, these findings could have implications for the use of antibiotics for minor illnesses in infancy

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ADHD Atten Deficit Hyperact Disord. 2017;9.

WHAT ARE THE BENEFITS OF METHYLPHENIDATE AS A TREATMENT FOR CHILDREN AND ADOLESCENTS WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER?

Gerlach M, Banaschewski T, Coghill D, et al.

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ADHD Atten Deficit Hyperact Disord. 2017;1-13.

PREPOTENT RESPONSE INHIBITION AND REACTION TIMES IN CHILDREN WITH ATTENTION DEFICIT/HYPERACTIVITY DISORDER FROM A CARIBBEAN COMMUNITY.

Jiménez-Figueroa G, Ardila-Duarte C, Pineda DA, et al.

Impairment in inhibitory control has been postulated as an underlying hallmark of attention deficit/hyperactivity disorder (ADHD), which can be utilized as a quantitative trait for genetic studies. Here, we evaluate whether inhibitory control, measured by simple automatized prepotent response (PR) inhibition variables, is a robust discriminant function for the diagnosis of ADHD in children and can be used as an endophenotype for future genetic studies. One hundred fifty-two school children (30.9% female, 67.8% with ADHD) were recruited. The ADHD checklist was used as the screening tool, whilst the DSM-IV Mini International Neuropsychiatry Interview, neurologic interview and neurologic examination, and the WISC III FSIQ test were administered as the gold standard procedure to assert ADHD diagnosis. A Go/No-Go task using a naturalistic and automatized visual signal was administered. A linear multifactor model (MANOVA) was fitted to compare groups including ADHD status, age, and gender as multiple independent factors. Linear discriminant analysis and the receiver operating characteristic curve were used to assess the predictive performance of PR inhibition variables for ADHD diagnosis. We found that four variables of prepotent response reaction time- and prepotent response inhibition established statistically significant differences between children with and without ADHD. Furthermore, these variables generated a strong discriminant function with a total classification capability of 73, 84% specificity, 68% sensitivity, and 90% positive predictive value for ADHD diagnosis, which support reaction times as a candidate endophenotype that could potentially be used in future ADHD genetic research

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Am J Orthopsychiatry. 2017.

ALCOHOL AND DRUG USE AMONG INTERNATIONALLY ADOPTED ADOLESCENTS: RESULTS FROM A NORWEGIAN POPULATION-BASED STUDY.

Askeland KG, Sivertsen B, Skogen JC, et al.

Internationally adopted adolescents are at increased risk for mental health problems. However, little is known about problematic alcohol and drug use, which are important indicators of maladjustment. The aim of this study was to examine the level of problematic alcohol and drug use in internationally adopted adolescents compared to their nonadopted peers. The study is based on data from the youth@hordaland-survey, which was conducted in Hordaland County, Norway, in the spring of 2012. All adolescents born from 1993 to 1995 residing in Hordaland at the time of the study were invited to participate. Information on adoption was obtained from the Central Adoption Registry and linked to self-report data from the youth@hordaland-survey. Among 10,200 participants, 45 were identified as internationally adopted. No significant differences were found between international adoptees and their peers regarding whether or not they had tried alcohol or illicit drugs or their patterns of drinking behavior. However, adopted adolescents had a higher mean score on a measure of problematic alcohol and drug use compared to their nonadopted peers. The difference was attenuated and no longer significant when adjusting for measures of depression and attention-deficit/hyperactivity disorder. Results from a structural equation model indicated a full mediation effect of mental health problems on the association between adoption status and problematic alcohol and drug use. Our findings indicate that internationally adopted adolescents experience more problematic alcohol and drug use than their nonadopted peers, and the difference can largely be explained by mental health problems

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Ann Gen Psychiatry. 2017;16.

PREVALENCE AND EFFECT OF ATTENTION-DEFICIT/HYPERACTIVITY DISORDER ON SCHOOL PERFORMANCE AMONG PRIMARY SCHOOL PUPILS IN THE HOHOE MUNICIPALITY, GHANA.

Afeti K, Nyarko SH.

Background: Attention-deficit/hyperactivity disorder (ADHD) is one of the most common disorders in early childhood. However, not many studies have been conducted on the prevalence and effect of ADHD on school performance in Ghana. This study sought to ascertain the prevalence of ADHD and its effect on school performance among primary school pupils in the Hohoe municipality of Ghana.

Methods: This is a cross-sectional descriptive study that included 400 primary school pupils in the Hohoe Municipality of Ghana. The study adopted the disruptive behaviour disorder rating scale which includes the three subtypes of ADHD among pupils in the form of a close-ended questionnaire for data collection.

Results: The results revealed the overall prevalence of ADHD to be 12.8%. The males had a higher prevalence (14.4%) compared to the females (10.5%). For the subtypes, the prevalence was 8.0% for attention-deficit disorder, 8.5% for hyperactivity disorder and 3.8% for the combined subtype. In terms of school performance, the results showed that there was a significant difference in the school performance between ADHD-positive pupils and the negative status pupils among the various core subjects.

Conclusions: Attention-deficit/hyperactivity disorder was quite prevalent among primary school pupils in the Hohoe Municipality, and has impacted negatively on their school performance. Screening of pupils for ADHD should be integrated into the school health services to enable early detection and management

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Arch Clin Neuropsychol. 2017 Feb;32:117-22.

FACTOR STRUCTURE OF IMPACT(R) IN ADOLESCENT STUDENT ATHLETES.

Gerrard PB, Iverson GL, Atkins JE, et al.

OBJECTIVE: ImPACT(R) (Immediate Post-Concussion Assessment and Cognitive Testing) is a computerized neuropsychological screening battery, which is widely used to measure the acute effects of sport-related concussion and to monitor recovery from injury. This study examined the factor structure of ImPACT(R) in several samples of high school student athletes. We hypothesized that a 2-factor structure would be present in all samples.

METHOD: A sample of 4,809 adolescent student athletes was included, and subgroups with a history of treatment for headaches or a self-reported history of learning problems or attention-deficit hyperactivity disorder were analyzed separately. Exploratory principal axis factor analyses with Promax rotations were used.
RESULTS: As hypothesized, both the combination of Verbal Memory and Visual Memory Composite scores loaded on one (Memory) factor, while Visual Motor Speed and Reaction Time loaded on a different (Speed) factor, in the total sample and in all subgroups.
CONCLUSION: These results provide reasonably compelling evidence, across multiple samples, which ImPACT(R) measures 2 distinct factors: memory and speed

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Arch Clin Neuropsychol. 2017 Feb;32:81-93.
USEFULNESS AND VALIDITY OF CONTINUOUS PERFORMANCE TESTS IN THE DIAGNOSIS OF ATTENTION-DEFICIT HYPERACTIVITY DISORDER CHILDREN.
Berger I, Slobodin O, Cassuto H.
OBJECTIVE: Despite the popularity of continuous performance tests (CPT) in supporting the diagnostic procedure of attention-deficit hyperactivity disorder (ADHD), these measures are still controversial mainly due to limited sensitivity, specificity, and ecological validity. Thus, there continues to be a need for further validation of these objective attention measures. The purpose of this study was to evaluate the usefulness of a CPT that includes environmental distracting stimuli, in supporting the diagnosis of ADHD in children.
METHOD: Participants were 798 children aged 7-12 years (493 boys and 305 girls). The ADHD group included 339 children, whereas the control group included 459 children without ADHD. The study employed the MOXO-CPT, which incorporates visual and auditory stimuli serving as environmental distractors.
RESULTS: Compared to their unaffected peers, children with ADHD received significantly lower scores in all 4 CPT indices: attention, timing, hyperactivity, and impulsivity. Specifically, ADHD children were less attended to the stimuli and performed fewer reactions on accurate timing. Furthermore, children with ADHD performed significantly more impulsive and hyperactive responses than controls. Receiver operating characteristic analysis revealed fair to excellent diagnostic ability of all CPT indices except impulsivity, which showed poor ability to distinguish ADHD children from controls. The test's total score yielded excellent diagnostic performance.
CONCLUSIONS: MOXO-CPT consistently distinguished between children with ADHD and their unaffected peers, so that children with ADHD performed worse than controls in all study indices. Integration of CPT indices improves the diagnostic capacity of ADHD and may better reflect the complexity and heterogeneity of ADHD

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Asian J Psychiatr. 2017 Feb;25:147-53.
PREFRONTAL OXYGENATION DURING VERBAL FLUENCY AND COGNITIVE FUNCTION IN ADOLESCENTS WITH BIPOLAR DISORDER TYPE II.
Ono Y, Kikuchi M, Nakatani H, et al.
Evaluation of depressive states in children can be challenging. Most of the studies that have investigated cognitive function and cerebral blood volume changes using functional MRI (fMRI) in bipolar disorder (BD) have been confined to BDI or heterogeneous cohorts with attention-deficit/hyperactivity disorder (ADHD). This study investigated cognitive functions in adolescents with BDII and without ADHD using near-infrared spectroscopy (NIRS) and a Das-Naglieri Cognitive Assessment System (DN-CAS). Ten patients with BDII and without ADHD symptoms and 10 age- and gender-matched healthy controls were enrolled in the present study. NIRS was used to detect hemoglobin concentration changes during a verbal fluency test (VFT). In addition, the DN-CAS was used to evaluate cognitive function in four domains: planning, attention, simultaneous, and successive processing. Significant differences between the BDII and control groups in [oxy-Hb] changes during the early phase of VFT were observed in the lower prefrontal cortex but not in

cognitive functioning. Furthermore, there was a significant correlation between planning and attention scores in BD subjects

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Atten Defic Hyperact Disord. 2017 Mar;9:47-65.

THE DESCRIPTIVE EPIDEMIOLOGY OF DSM-IV ADULT ADHD IN THE WORLD HEALTH ORGANIZATION WORLD MENTAL HEALTH Surveys.

Fayyad J, Sampson NA, Hwang I, et al.

We previously reported on the cross-national epidemiology of ADHD from the first 10 countries in the WHO World Mental Health (WMH) Surveys. The current report expands those previous findings to the 20 nationally or regionally representative WMH surveys that have now collected data on adult ADHD. The Composite International Diagnostic Interview (CIDI) was administered to 26,744 respondents in these surveys in high-, upper-middle-, and low-/lower-middle-income countries (68.5% mean response rate). Current DSM-IV/CIDI adult ADHD prevalence averaged 2.8% across surveys and was higher in high (3.6%)- and upper-middle (3.0%)- than low-/lower-middle (1.4%)-income countries. Conditional prevalence of current ADHD averaged 57.0% among childhood cases and 41.1% among childhood subthreshold cases. Adult ADHD was significantly related to being male, previously married, and low education. Adult ADHD was highly comorbid with DSM-IV/CIDI anxiety, mood, behavior, and substance disorders and significantly associated with role impairments (days out of role, impaired cognition, and social interactions) when controlling for comorbidities. Treatment seeking was low in all countries and targeted largely to comorbid conditions rather than to ADHD. These results show that adult ADHD is prevalent, seriously impairing, and highly comorbid but vastly under-recognized and undertreated across countries and cultures

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Biological Trace Element Research. 2017;1-10.

HAIR ZINC AND SEVERITY OF SYMPTOMS ARE INCREASED IN CHILDREN WITH ATTENTION DEFICIT AND HYPERACTIVITY DISORDER: A HAIR MULTI-ELEMENT PROFILE STUDY.

Tippairote T, Temviriyanukul P, Benjapong W, et al.

Determination of bioelement levels in hair is an emerging non-invasive approach for screening bioelement deposition. However, the role of essential bioelement levels in hair and attention deficit/hyperactivity disorder (ADHD) risk or severity is largely unknown. In this study, we have compared multi-element hair profiles between healthy and ADHD Thai children. In addition, the correlations between bioelements and ADHD symptoms according to Diagnostic and Statistical Manual of Mental Disorders, 5th edition, diagnostic criteria were identified. A case-control study was conducted in 111 Thai children (45 newly diagnosed ADHD and 66 matched healthy), aged 3–7 years, living in Bangkok and suburban areas. Levels of 39 bioelements in hair were measured by ICP-MS. Among the analyzed bioelements, Cu/Zn and P/Zn ratios in ADHD children were significantly lower than those in healthy children. Indeed, increased hair Zn level was correlated with more symptoms of inattention, hyperactivity, and total ADHD symptoms. Higher Zn content was also associated with being female and older age. Furthermore, Zn in hair was positively correlated with levels of Ca, Mg, and P; however, it showed a negative correlation with Al, As, Fe, and Mo. These findings warrant further confirmation in a large-scale study. Thai Clinical Trials Registry (TCTR) study ID: 20151113001

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Biomed Res Int. 2017;2017:3513281.

A Randomized Trial of Comparing the Efficacy of Two Neurofeedback Protocols for Treatment of Clinical and Cognitive Symptoms of ADHD: Theta Suppression/Beta Enhancement and Theta Suppression/Alpha Enhancement.

Mohagheghi A, Amiri S, Moghaddasi BN, et al.

Introduction. Neurofeedback (NF) is an adjuvant or alternative therapy for children with Attention Deficit Hyperactivity Disorder (ADHD). This study intended to compare the efficacy of two different NF protocols on clinical and cognitive symptoms of ADHD.

Materials and Methods. In this clinical trial, sixty children with ADHD aged 7 to 10 years old were randomly grouped to receive two different NF treatments (theta suppression/beta enhancement protocol and theta suppression/alpha enhancement protocol). Clinical and cognitive assessments were conducted prior to and following the treatment and also after an eight-week follow-up.

Results. Both protocols alleviated the symptoms of ADHD in general ($p < 0.001$), hyperactivity ($p < 0.001$), inattention ($p < 0.001$), and omission errors ($p < 0.001$); however, they did not affect the oppositional and impulsive scales nor commission errors. These effects were maintained after an eight-week intervention-free period. The only significant difference between the two NF protocols was that high-frequency alpha enhancement protocol performed better in suppressing omission errors ($p < 0.001$).

Conclusion. The two NF protocols with theta suppression/beta enhancement and theta suppression/alpha enhancement have considerable and comparable effect on clinical symptoms of ADHD. Alpha enhancement protocol was more effective in suppressing omission errors

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BMC Med. 2017;15.

A unique pattern of cortical connectivity characterizes patients with attention deficit disorders: A large electroencephalographic coherence study.

Duffy FH, Shankardass A, McAnulty GB, et al.

Background Attentional disorders (ADD) feature decreased attention span, impulsivity, and over-activity interfering with successful lives. Childhood onset ADD frequently persists to adulthood. Etiology may be hereditary or disease associated. Prevalence is 5% but recognition may be 'overshadowed' by comorbidities (brain injury, mood disorder) thereby escaping formal recognition. Blinded diagnosis by MRI has failed. ADD may not itself manifest a single anatomical pattern of brain abnormality but may reflect multiple, unique responses to numerous and diverse etiologies. Alternatively, a stable ADD-specific brain pattern may be better detected by brain physiology. EEG coherence, measuring cortical connectivity, is used to explore this possibility.

Methods Participants: Ages 2 to 22 years; 347 ADD and 619 neurotypical controls (CON). Following artifact reduction, principal components analysis (PCA) identifies coherence factors with unique loading patterns. Discriminant function analysis (DFA) determines discrimination success differentiating ADD from CON. Split-half and jackknife analyses estimate prospective diagnostic success. Coherence factor loading constitutes an ADD-specific pattern or 'connectome'.

Results PCA identified 40 factors explaining 50% of total variance. DFA on CON versus ADD groups utilizing all factors was highly significant ($p \leq 0.0001$). ADD subjects were separated into medication and comorbidity subgroups. DFA (stepping allowed) based on CON versus ADD without comorbidities or medication treatment successfully classified the correspondingly held out ADD subjects in every instance. Ten randomly generated split-half replications of the entire population demonstrated high-average classification success for each of the left out test-sets (overall: CON, 83.65%; ADD, 90.07%). Higher success was obtained with more restricted age sub-samples using jackknifing: 2-8 year olds (CON, 90.0%; ADD, 90.6%); 8-14 year olds (CON, 96.8%; ADD 95.9%); and 14-20 year-olds (CON, 100.0%; ADD, 97.1%). The connectome manifested decreased and increased coherence. Patterns were complex and bi-hemispheric; typically reported front-back and left-right loading patterns were not observed. Subtemporal electrodes (seldom utilized) were prominently involved.

Conclusions Results demonstrate a stable coherence connectome differentiating ADD from CON subjects including subgroups with and without comorbidities and/or medications. This functional 'connectome', constitutes a diagnostic ADD phenotype. Split-half replications support potential for EEG-based ADD

diagnosis, with increased accuracy using limited age ranges. Repeated studies could assist recognition of physiological change from interventions (pharmacological, behavioral).

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Br J Clin Psychol. 2017 Mar;56:33-52.

FATIGUE IN AN ADULT ATTENTION DEFICIT HYPERACTIVITY DISORDER POPULATION: A TRANS-DIAGNOSTIC APPROACH.

Rogers DC, Dittner AJ, Rimes KA, et al.

OBJECTIVES: Trans-diagnostic approaches suggest that key cognitive and behavioural processes maintain symptoms across a wide range of mental health disorders. Fatigue is a common clinical feature of attention deficit hyperactivity disorder (ADHD) in adulthood; however, empirical data supporting its prevalence are lacking. This study aimed to collate outcomes from outpatient services to (1) investigate the prevalence of fatigue in adults with ADHD, (2) examine symptoms of ADHD in adults with chronic fatigue syndrome (CFS), and (3) consider secondary clinical characteristics common to both disorder groups.
METHODS: Measures of self-reported fatigue were compared across groups of adults with ADHD (N = 243), CFS (N = 86), and healthy controls (HC) (N = 211) using a between-subjects cross-sectional design. Groups were also compared on secondary clinical measures of functional impairment, mood, anxiety, sleep, self-efficacy, and their beliefs about the acceptability of expressing emotions.
RESULTS: The ADHD group were significantly more fatigued than HC with 62% meeting criteria for fatigue caseness. ADHD symptoms were significantly greater in the CFS group than in HC. ADHD and CFS groups did not differ significantly on measures of functional impairment, mood, and self-efficacy. No significant differences were detected on measures of anxiety when items relating to physical restlessness were removed from the analysis.
CONCLUSIONS: Adults with ADHD experience greater fatigue than HC. Adults with CFS and ADHD share many trans-diagnostic clinical characteristics, including difficulties with low mood, anxiety, and reduced self-efficacy, which impact upon their overall functioning. Further research is required to investigate extraneous factors mediating fatigue severity in these clinical groups. PRACTITIONER POINTS: Fatigue is a common clinical feature of attention deficit hyperactivity disorder (ADHD) in adulthood. Evidence-based interventions for chronic fatigue syndrome could be adapted to address fatigue in ADHD in adults

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Brain Dev. 2017.

INCREASED CORTISOL AWAKENING RESPONSE AFTER COMPLETING THE SUMMER TREATMENT PROGRAM IN CHILDREN WITH ADHD.

Okabe R, Okamura H, Egami C, et al.

Objective: Little is known about the cortisol awakening response (CAR) in children with attention deficit hyperactivity disorder (ADHD). Here, we examined the CAR in children with ADHD and their mothers before, immediately after, and 4. months after an intensive summer treatment program (STP).
Methods: Participants were 37 children aged 7-12years who completed the STP in 2009 and 2010, and their mothers. Daily saliva samples for cortisol measurement were collected twice daily at awakening and 30min afterwards at pre-STP, post-STP, and during a follow-up measurement period. ADHD symptom scores were evaluated by parents, and participants completed the Kid-KINDLR QOL questionnaire.
Results: CAR was low in children with ADHD before the STP, and increased to the control range 4months after STP. Maternal CAR also tended to increase after STP. Changes in the CAR in children tended to correlate with an improved ADHD inattention scores (p =0.091), physical health (p =0.070), and school life subscales scores in the Kid-KINDLR (p =0.079).
Conclusion: We demonstrated that STP improved the behavior and QOL of children with ADHD. Our results indicate that STP could lead to improvements in HPA axis function, as reflected by increased CAR after STP

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Brain Imaging Behav. 2017;1-11.

THE EFFECTS OF GRIN2B AND DRD4 GENE VARIANTS ON LOCAL FUNCTIONAL CONNECTIVITY IN ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.

Kim JI, Yoo JH, Kim D, et al.

Based on the interplay between dopaminergic and glutamatergic systems, N-Methyl-D-Asparate (NMDA) receptor genes are thought to be involved in the pathophysiology of ADHD. However, the phenotypical correlates of brain functions associated with NMDA receptor genes and dopamine receptor genes in ADHD are yet to be investigated. We examined the diagnosis, genotype and the diagnosis-genotype interaction effects of GRIN2B and DRD4 variants on the local functional connectivity (by using the mean of static regional homogeneity (ReHo) and the mean and standard deviation (SD) of dynamic ReHo) in 67 ADHD subjects and 44 controls (aged 6–17 years). GRIN2B genotypes were divided into the C/C group and T allele carrier group; DRD4 genotypes were divided into the 2R group and non-2R group. The correlation between the ReHo values showing significant diagnosis-genotype interaction and ChildrenΓÇÖs Color Trails Test (CCTT) scores were examined. CCTT measures processing speed, sustained and divided attention. There were significant diagnosis ($p < 0.001$) and interaction ($p = 0.02$) effects of the GRIN2B variant on the static ReHo mean in the left superior parietal cluster, and the ReHo value was positively correlated with the CCTT interference score in the ADHD with T allele carrier subgroup ($p = 0.012$). There were significant diagnosis ($p < 0.001$) and interaction ($p = 0.03$) effects of the DRD4 variant on the dynamic ReHo SD in the right superior parietal cluster. These results suggest that alterations in the glutamate and dopamine system in ADHD may contribute to abnormalities in local functional connectivity and its dynamic repertoire in the superior parietal area, and these abnormalities would be related to dysfunction in sustained and divided attention

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Brain Imaging Behav. 2017;1-9.

LONG-TERM EFFECTS OF STIMULANT EXPOSURE ON CEREBRAL BLOOD FLOW RESPONSE TO METHYLPHENIDATE AND BEHAVIOR IN ATTENTION-DEFICIT HYPERACTIVITY DISORDER.

Schrantee A, Bouziane C, Bron EE, et al.

Stimulant prescription rates for attention deficit hyperactivity disorder (ADHD) are increasing, even though potential long-term effects on the developing brain have not been well-studied. A previous randomized clinical trial showed short-term age-dependent effects of stimulants on the DA system. We here assessed the long-term modifying effects of age-of-first-stimulant treatment on the human brain and behavior. 81 male adult ADHD patients were stratified into three groups: 1) early stimulant treatment (EST; <16 years of age) 2) late stimulant treatment (LST: ΓëÑ23 years of age) and 3) stimulant treatment naive (STN; no history of stimulant treatment). We used pharmacological magnetic resonance imaging (phMRI) to assess the cerebral blood flow (CBF) response to an oral methylphenidate challenge (MPH, 0.5 mg/kg), as an indirect measure of dopamine function in fronto-striatal areas. In addition, mood and anxiety scores, and recreational drug use were assessed. Baseline ACC CBF was lower in the EST than the STN group ($p = 0.03$), although CBF response to MPH was similar between the three groups ($p = 0.23$). ADHD symptom severity was higher in the STN group compared to the other groups ($p < 0.01$). In addition, the EST group reported more depressive symptoms ($p = 0.04$), but not anxiety ($p = 0.26$), and less recreational drug use ($p = 0.04$). In line with extensive pre-clinical data, our data suggest that early, but not late, stimulant treatment long-lastingly affects the human brain and behavior, possibly indicating fundamental changes in the dopamine system

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Brain Stimul. 2017;10:517.

ANODAL TDCS OVER THE LEFT DLPFC IMPROVED WORKING MEMORY AND REDUCES SYMPTOMS IN CHILDREN WITH ADHD.

Siniatchkin M.

Anodal transcranial direct current stimulation (tDCS) of the prefrontal cortex has repeatedly been shown to improve working memory. As patients with attention deficit hyperactivity disorder (ADHD) are characterized

by both under activation of the prefrontal cortex and deficits in working memory that correlate with clinical symptoms, it is hypothesized that the modulation of prefrontal activity with tDCS in patients with ADHD increases performance in working memory and reduces symptoms of ADHD. In a randomized, double-blinded, sham-controlled study, 1mA anodal tDCS over the left dorsolateral prefrontal cortex (DLPFC) was applied on 5 consecutive days. Anodal tDCS caused a significant reduction in clinical symptoms of inattention and impulsivity in children with ADHD compared to sham stimulation. The clinical effects were supported by a significant reduction in inattention and hyperactivity in a standardized working memory test (QbTest). The described effects were more pronounced 7 days after the end of stimulation, a fact which emphasizes the long-lasting clinical and neuropsychological changes after tDCS. Moreover, the clinical and neuropsychological changes correlated with activation of neuronal networks of working memory and executive control following tDCS as revealed by functional MRI. This study highlights the potential of anodal tDCS of the left DLPFC as a form of treatment in patients with ADHD

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Brain Stimul. 2017;10:530-31.

IS THE RIGHT INFERIOR FRONTAL GYRUS A PROMISING TARGET FOR TDCS IN ADHD?

Krauel K, Breitling C, Dannhauer M, et al.

Most children and adolescents with ADHD are impaired in the suppression of task irrelevant, competing stimuli (interference control) and in the inhibition of prepotent responses. The brain region most prominently associated with these aspects of inhibition control is the right inferior frontal gyrus (rIFG) which shows structural and functional alterations in ADHD. In our talk, we will give an overview over different approaches using transcranial direct current stimulation (tDCS) of the rIFG in healthy adults and will present findings from two of our own studies with ADHD youth targeting the rIFG

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Brain Stimul. 2017;10:349.

BIOMARKERS OF BEHAVIORAL AND MOTOR CONTROL IN CHILDREN: TOURETTE SYNDROME, ADHD, ASD, AND NEUROPHARMACOLOGY.

Gilbert DL.

Introduction: The clinical heterogeneity of symptom-defined diagnoses in pediatric neurology and psychiatry, many of which result from combined polygenetic, epigenetic, and environmentally influenced factors, poses substantial challenges for understanding the neurobiological substrates of these conditions. Research into neural mechanisms is vital for identifying better treatments.

Methods: Dr. Donald Gilbert will review recent and ongoing neurostimulation studies of neurodevelopmental disorders.

Results: While standard studies have involved single and paired TMS pulses delivered at rest, an increasing variety of paradigms now can be used to study other questions in these populations. For example, studies integrating precisely timed TMS pulses into behavioral paradigms have explored neurophysiological underpinnings of response inhibition, and reward and motivation. Repetitive and theta-burst studies probe mechanisms of neuroplasticity. Blinded medication studies and studies in individuals with single-gene diseases provide additional clinically relevant information. Combinations of TMS studies with imaging techniques advance understanding through complementary approaches. Methods and data from recent studies exemplifying some of these newer TMS paradigms in children will be presented to highlight opportunities for clinically relevant discovery.

Discussion: Transcranial Magnetic Stimulation studies have improved understanding of the development of motor control in typically developing children as well as in children with a variety of developmental, psychiatric, and neurological conditions

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Can Fam Physician. 2016 Dec;62:979-82.

UNDERSTANDING ATTENTION DEFICIT HYPERACTIVITY DISORDER AS A CONTINUUM.

McLennan JD.

OBJECTIVE: To review research findings that consider whether attention deficit hyperactivity disorder (ADHD) is a discrete entity or whether it is more consistent with an extreme end-of-trait distribution in the population and to then grapple with the potential clinical implications.

QUALITY OF EVIDENCE: Peer-reviewed publications in the past 5 years, drawing from diverse fields (taxonomy, epidemiology, genetics, neurobiology, and neuropsychology), were identified through searches in MEDLINE and PsycINFO.

MAIN MESSAGE: Accumulating research findings are most consistent with a predominately dimensional rather than a qualitatively distinct existence for ADHD. This does not negate the clinical needs of those who have substantial ADHD symptom clusters, nor the risks that such symptoms entail. However, the lack of discontinuity in the distribution of such traits in the population creates great uncertainty as to what thresholds should prompt explicit intervention.

CONCLUSION: The implications of this pattern of findings might include the need to de-emphasize categorical conceptualizations of ADHD, produce evidence to better inform risk-benefit ratios of interventions along a spectrum of symptom and functional severity, and more coherently triage and arrange service delivery on the basis of symptom and functional severity rather than artificial diagnostic categorizations

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Child Adolesc Psychiatr Clin N Am. 2016 Jul;25:509-20.

INTERNET ADDICTION AND OTHER BEHAVIORAL ADDICTIONS.

Jorgenson AG, Hsiao RC, Yen CF.

The Internet is increasingly influential in the lives of adolescents. Although there are many positives, there are also risks related to excessive use and addiction. It is important to recognize clinical signs and symptoms of Internet addiction (compulsive use, withdrawal, tolerance, and adverse consequences), treat comorbid conditions (other substance use disorders, attention deficit hyperactivity disorder, anxiety, depression, and hostility), and initiate psychosocial interventions. More research on this topic will help to provide consensus on diagnostic criteria and further clarify optimal management

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Child Adolesc Psychiatr Clin North Am. 2017;26:311-27.

FACILITATING TRANSITION FROM HIGH SCHOOL AND SPECIAL EDUCATION TO ADULT LIFE: FOCUS ON YOUTH WITH LEARNING DISORDERS, ATTENTION-DEFICIT/HYPERACTIVITY DISORDER, AND SPEECH/LANGUAGE IMPAIRMENTS.

Ascherman LI, Shaftel J.

Youth with learning disorders, speech/language disorders, and/or attention-deficit/hyperactivity disorder may experience significant struggles during the transition from high school to postsecondary education and employment. These disorders often occur in combination or concurrently with behavioral and emotional difficulties. Incomplete evaluation may not fully identify the factors underlying academic and personal challenges. This article reviews these disorders, the role of special education law for transitional age youth in public schools, and the Americans with Disabilities Act in postsecondary educational and employment settings. The role of the child and adolescent psychiatrist and the importance of advocacy for these youth are presented

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Child Neuropsychol. 2017;1-24.

SEQUENCED NEUROCOGNITIVE AND BEHAVIORAL PARENT TRAINING FOR THE TREATMENT OF ADHD IN SCHOOL-AGE CHILDREN.

Chacko A, Bedard ACV, Marks D, et al.

The present study examines the potential of sequencing a neurocognitive intervention with behavioral parent training (BPT) to improve executive functions (EFs), psychiatric symptoms, and multiple indices of functional impairment in school-age children aged 7 to 11 years who have been diagnosed with attention-deficit/hyperactivity disorder (ADHD). Specifically, in a randomized controlled trial design, 85 children were assigned to either Cogmed Working Memory Training (CWMT) followed by an empirically supported, manualized BPT intervention, or to a placebo version of CWMT followed by the same BPT intervention. Working memory maintenance (i.e., attention control/short-term memory), working memory processing and manipulation, ADHD and oppositional defiant disorder (ODD) symptoms, impairment in parent's child dynamics, familial impairment, and overall functional compromise were evaluated as outcomes. The results suggest specific effects of the combined CWMT and BPT program on verbal and nonverbal working memory storage and nonverbal working memory processing and manipulation but no incremental benefits in regard to ADHD symptoms, ODD symptoms, and functional outcomes. The present findings do not support the hypothesis regarding the complementary and augmentative benefits of sequenced neurocognitive and BPT interventions for the treatment of ADHD. These results, the study's limitations, and future directions for research are further discussed

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Child Neuropsychol. 2017;23:483-501.

A RATING MEASURE OF ADHD-RELATED NEUROPSYCHOLOGICAL IMPAIRMENT IN CHILDREN AND ADOLESCENTS: DATA FROM THE COGNITION AND MOTIVATION IN EVERYDAY LIFE (CAMEL) SCALE FROM POPULATION AND CLINICAL SAMPLES.

Van Liefferinge D, Sonuga-Barke E, Van Broeck N, et al.

A new parent-completed questionnaire, the Cognition and Motivation in Everyday Life (CAMEL) scale, was developed to provide a comprehensive assessment of neuropsychological impairment in children related to attention-deficit/hyperactivity disorder (ADHD) across diverse cognitive, motivational and energetic domains. Its psychometric properties were investigated. A total of 60 items were generated to cover a wide range of putative ADHD-related neuropsychological processes. A clinical (n-á=-á142) and community (n-á=-á810) sample of parents with children between 6 and 16-áyears of age completed the questionnaire. Data on ADHD symptoms were also collected with a commonly-used, validated parent rating scale to explore the associations between CAMEL scores and dimensional measures of child ADHD and conduct problems. Factor analysis identified six factors which we labeled (i) Cognition, (ii) Self-Direction and Organization, (iii) Effort Engagement, (iv) Arousal Regulation, (v) Motivational Responsiveness, and (vi) Cautiousness. Self-Direction and Organization and Arousal Regulation were the strongest predictors for ADHD symptomatology. Self-Direction and Organization was strongly associated with inattention and Arousal Regulation with hyperactivity-impulsivity symptoms. Parents distinguished between broad neuropsychological domains in reliable and plausible ways, making distinctions between key aspects of functioning. However, the boundaries between these domains did not map directly onto the distinctions drawn within traditional models of ADHD deficits. Further research is required to examine the predictive validity and cost-effectiveness of the CAMEL scale compared to direct objective testing using laboratory measures in predicting prognosis and treatment outcome

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Chin Med J (Engl). 2016 May;129:1022-27.

DEEP BRAIN STIMULATION OF THE GLOBUS PALLIDUS INTERNUS IN PATIENTS WITH INTRACTABLE TOURETTE SYNDROME: A 1-YEAR FOLLOW-UP STUDY.

Zhang XH, Li JY, Zhang YQ, et al.

BACKGROUND: Deep brain stimulation (DBS) has been a promising treatment for patients with refractory Tourette syndrome (TS) for more than a decade. Despite successful DBS treatment of TS in more than 100 patients worldwide, studies with a large patient sample and long-term follow-up assessments are still scarce. Accordingly, we investigated the clinical efficacy and safety of globus pallidus internus (GPi) DBS in the treatment of intractable TS in 24 patients with a 1-year follow-up assessment.

METHODS: Bilateral/unilateral GPi-DBS was performed in 24 patients with TS. We evaluated symptoms of tics and obsessive-compulsive disorder (OCD) through the Yale Global Tic Severity Scale (YGTSS) and Yale-Brown Obsessive-compulsive Scale (Y-BOCS). We used the Wechsler Adult Intelligence Scale-Revised in China (WAIS-RC) to evaluate the safety of the treatment. We conducted follow-up assessments of all patients for at least 12 months (12-99 months).

RESULTS: Symptoms of tics and OCD were significantly relieved at a 12-month follow-up assessment. The mean YGTSS score was 74.04 ± 11.52, 49.83 ± 10.91, 32.58 ± 7.97, and 31.21 ± 8.87 at baseline, 3, 6, and 12 months, respectively. The mean YGTSS scores obtained at the follow-up assessments were significantly different from the baseline ($P < 0.05$). The improvement in motor tics was superior to that in phonic tics. The mean Y-BOCS scores were 21.61 ± 4.97, 18 ± 4.58, 14.39 ± 3.99, and 13.78 ± 4.56 at baseline, 3, 6, and 12 months, respectively ($P < 0.05$). We observed a remarkable improvement in psychiatric comorbidities, such as OCD and attention-deficit hyperactivity disorder, after the procedure. WAIS-RC scores were comparable before and after the operation. There were no severe postoperative complications.

CONCLUSION: GPi-DBS appears to comprehensively alleviate tic symptoms and psychiatric comorbidities in patients with TS, thus significantly improving patients' quality of life

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Chin Med J (Engl). 2017 Mar;130:549-58.

EXECUTIVE FUNCTION TRAINING FOR CHILDREN WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER.

Shuai L, Daley D, Wang YF, et al.

BACKGROUND: Accumulating evidence indicates that attention deficit hyperactivity disorder (ADHD) is associated with core deficits in executive function (EF) which predicts poorer academic and occupational functioning. This makes early intervention targeting EF impairments important to prevent long-term negative outcomes. Cognitive training is a potential ADHD treatment target. The present study aimed to explore the efficacy, feasibility, and acceptability of a cognitive training program (targeting child's multiple EF components and involving parent support in daily life), as a nonpharmacological intervention for children with ADHD.

METHODS: Forty-four school -age children with ADHD and their parents participated in 12 sessions of EF training (last for 12 weeks) and 88 health controls (HC) were also recruited. Training effects were explored using both neuropsychological tests (Stroop color-word test, Rey-Osterrieth complex figure test, trail making test, tower of Hanoi, and false-belief task) and reports of daily life (ADHD rating scale-IV, Conners' parent rating scale, and behavior rating inventory of executive function [BRIEF]) by analysis of paired sample t-test and Wilcoxon signed-rank test. The differences on EF performances between children with ADHD after training and HC were explored using multivariate analysis.

RESULTS: The results (before vs. after EF training) showed that after intervention, the children with ADHD presented better performances of EF both in neuropsychological tests (word interference of Stroop: 36.1 ± 14.6 vs. 27.1 ± 11.1, $t = 4.731$, $P < 0.001$; shift time of TMT: 194.9 ± 115.4 vs. 124.8 ± 72.4, $Z = -4.639$, $P < 0.001$; false-belief task: $\chi 2 = 6.932$, $P = 0.008$) and reports of daily life (global executive composite of BRIEF: 148.9 ± 17.5 vs. 127.8 ± 17.5, $t = 6.433$, $P < 0.001$). The performances on EF tasks for children with ADHD after EF training could match with the level of HC children. The ADHD symptoms (ADHD rating scale total score: 32.4 ± 8.9 vs. 22.9 ± 8.2, $t = 6.331$, $P < 0.001$) and behavioral problems of the children as reported by parents also reduced significantly after the intervention. Participants reported that the EF training program was feasible to administer and acceptable.

CONCLUSIONS: The EF training program was feasible and acceptable to children with ADHD and parents. Although replication with a larger sample and an active control group are needed, EF training program with

multiple EF focus and parent involving in real-life activities could be a potentially promising intervention associated with significant EF (near transfer) and ADHD symptoms improvement (far transfer)

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Clin EEG Neurosci. 2017 Jan;48:20-32.

QUANTITATIVE EEG IN CHILDREN AND ADULTS WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER: COMPARISON OF ABSOLUTE AND RELATIVE POWER SPECTRA AND THETA/BETA RATIO.

Markovska-Simoska S, Pop-Jordanova N.

In recent decades, resting state electroencephalographic (EEG) measures have been widely used to document underlying neurophysiological dysfunction in attention deficit hyperactivity disorder (ADHD). Although most EEG studies focus on children, there is a growing interest in adults with ADHD too. The aim of this study was to objectively assess and compare the absolute and relative EEG power as well as the theta/beta ratio in children and adults with ADHD. The evaluated sample comprised 30 male children and 30 male adults with ADHD diagnosed according to DSM-IV criteria. They were compared with 30 boys and 30 male adults matched by age. The mean age (±SD) of the children's group was 9 (±2.44) years and the adult group 35.8 (±8.65) years. EEG was recorded during an eyes-open condition. Spectral analysis of absolute (muV2) and relative power (%) was carried out for 4 frequency bands: delta (2-4 Hz), theta (4-8 Hz), alpha (8-13 Hz), and beta (13-21 Hz). The findings obtained for ADHD children are increased absolute power of slow waves (theta and delta), whereas adults exhibited no differences compared with normal subjects. For the relative power spectra there were no differences between the ADHD and control groups. Across groups, the children showed greater relative power than the adults in the delta and theta bands, but for the higher frequency bands (alpha and beta) the adults showed more relative power than children. Only ADHD children showed greater theta/beta ratio compared to the normal group. Classification analysis showed that ADHD children could be differentiated from the control group by the absolute theta values and theta/beta ratio at Cz, but this was not the case with ADHD adults. The question that should be further explored is if these differences are mainly due to maturation processes or if there is a core difference in cortical arousal between ADHD children and adults

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Clin Neuropharmacol. 2017 Jan;40:11-15.

NO SUPERIORITY OF TREATMENT WITH OSMOTIC CONTROLLED-RELEASE ORAL DELIVERY SYSTEM-METHYLPHENIDATE OVER SHORT/MEDIUM-ACTING METHYLPHENIDATE PREPARATIONS IN THE RATE AND TIMING OF INJURIES IN CHILDREN WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.

Golubchik P, Kodesh A, Weizman A.

OBJECTIVES: Methylphenidate (MPH) treatment in patients with attention-deficit/hyperactivity disorder (ADHD) is reported to reduce the risk for injuries. In the present study, the rate and timing of injuries were compared among the various MPH preparations (4 and 6-8 vs 12 hour-acting) in children with ADHD.

METHODS: This real-world retrospective study covered the years 2011 to 2013. Participants included 2042 youngsters (aged 4-18 years, 13.01 ± 3.2 years; 71.8% males and 28.2% females) diagnosed with ADHD according to the International Statistical Classification of Diseases, 10th Revision criteria and treated with various MPH preparations. They were divided into 2 groups by their treatment preparation as follows: MPH-immediate release (MPH-IR)-4 hour-acting pooled with MPH-slow release/long-acting (MPH-SR/LA)- 6 to 8 hour-acting versus osmotic controlled-release oral delivery system-MPH (OROS-MPH; Concerta)-12 hour-acting that consisted of pooling of OROS-MPH only and OROS-MPH combined with the other MPH preparations. The monthly rates of injury, specifically, late injury (occurrence between 4:00 p.m. to midnight) and for multiple injuries, the time interval between injuries, were assessed.

RESULTS: No significant differences in monthly rate of nonfatal injuries were found between OROS-MPH with or without 4/6 to 8 hour-acting MPH-formulations versus only 4/6 to 8 hour-acting MPH-preparations (P = 0.53). Neither were differences found in the between-injury time interval (P = 0.83) or in late-injury-rates (P = 0.37) between those groups.

CONCLUSIONS: This real-world-naturalistic study in the community demonstrates that, in ADHD pediatric populations, OROS-MPH preparation is not superior to short/medium-acting (4/6-8 hours) MPH preparations regarding the rate and timing of injuries

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Clin Ter. 2016 Nov;167:191-97.

POLLUTION, THE THYROID AND NEURODEVELOPMENT.

Ozzola G.

The global prevalence of neurodevelopmental diseases is on the rise. The number of autistic babies in the US has jumped from 1 in 68 to 1 in 42. Plus more and more children have attention disorders or hyperactivity disorders. The genetic causes of these disorders of neurological development cannot explain such radical increases in the incidence and this leads one to look for the culprit in other elements, many of which have been shown to disrupt normal thyroid function. For instance, many polluting chemical substances can interfere with thyroid hormone (TH) metabolism and this might lead to abnormalities in the neurological development of the fetus or the child

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Clin Neurophysiol. 2017;128:529-37.

TO MAKE A MOLEHILL OUT OF A MOUNTAIN: AN ERP-STUDY ON COGNITIVE REAPPRAISAL OF NEGATIVE PICTURES IN CHILDREN WITH AND WITHOUT ADHD.

van Cauwenberge V, El Kaddouri R, Hoppenbrouwers K, et al.

Objective We investigated cognitive reappraisal in children with ADHD by means of the late positive potential (LPP) and self-report ratings. We expected diminished LPP modulation following reappraisal and lower self-report scores in children with ADHD. Methods Eighteen children with ADHD and 24 typically developing (TD) children (8–12 years) performed a cognitive reappraisal task, while EEG was recorded, and filled out a questionnaire on cognitive reappraisal. Results Despite the lack of main reappraisal effects on LPP, the LPP was less positively modulated during reappraisal in ADHD compared to TD children. Conclusions Children with ADHD reported less use of reappraisal and could be distinguished from TD children based on LPP modulation. However the lack of main effects of reappraisal on LPP in both groups hinders clear interpretation of this finding and questions the suitability of LPP modulation within the current paradigm as a neural index of reappraisal in children 8–12 years old, and warrants further research on the inter-individual variability and sensitivity of LPP modulation as a neural index of emotion regulation in children. Significance This is the first study investigating the LPP during cognitive reappraisal in children with ADHD

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Clin Psychopharmacol Neurosci. 2017;15:9-18.

SLEEP PROBLEMS AS PREDICTORS IN ATTENTION-DEFICIT HYPERACTIVITY DISORDER: CAUSAL MECHANISMS, CONSEQUENCES AND TREATMENT.

Um YH, Hong SC, Jeong JH.

Attention-deficit hyperactivity disorder (ADHD) is notorious for its debilitating consequences and early age of onset. The need for early diagnosis and intervention has frequently been underscored. Previous studies have attempted to clarify the bidirectional relationship between ADHD and sleep problems, proposing a potential role for sleep problems as early predictors of ADHD. Sleep deprivation, sleep-disordered breathing, and circadian rhythm disturbances have been extensively studied, yielding evidence with regard to their induction of ADHD-like symptoms. Genetic-phenotypic differences across individuals regarding the aforementioned sleep problems have been elucidated along with the possible use of these characteristics for early prediction of ADHD. The long-Term consequences of sleep problems in individuals with ADHD include obesity, poor academic performance, and disrupted parent-child interactions. Early intervention has been proposed as an

approach to preventing these debilitating outcomes of ADHD, with novel treatment approaches ranging from melatonin and light therapy to myofunctional therapy and adjustments of the time point at which school starts

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CNS Drugs. 2017;31:199-215.

CARDIOVASCULAR EFFECTS OF STIMULANT AND NON-STIMULANT MEDICATION FOR CHILDREN AND ADOLESCENTS WITH ADHD: A SYSTEMATIC REVIEW AND META-ANALYSIS OF TRIALS OF METHYLPHENIDATE, AMPHETAMINES AND ATOMOXETINE.

Hennissen L, Bakker MJ, Banaschewski T, et al.

Background: Many children and adolescents with attention deficit/hyperactivity disorder (ADHD) are treated with stimulant and non-stimulant medication. ADHD medication may be associated with cardiovascular effects. It is important to identify whether mean group effects translate into clinically relevant increases for some individual patients, and/or increase the risk for serious cardiovascular adverse events such as stroke or sudden death.

Objectives: To evaluate potential cardiovascular effects of these treatments, we conducted a systematic review and meta-analysis of the effects of methylphenidate (MPH), amphetamines (AMP), and atomoxetine (ATX) on diastolic and systolic blood pressure (DBP, SBP) and heart rate (HR) in children and adolescents with ADHD.

Methods: We conducted systematic searches in electronic databases (PsychINFO, EMBASE and Medline) to identify published trials which involved individuals who were (i) diagnosed with ADHD and were aged between 0–18-áyears; (ii) treated with MPH, AMP or ATX and (iii) had their DBP and SBP and/or HR measured at baseline (pre) and the endpoint (post) of the study treatment. Studies with an open-label design or a double-blind randomised control design of any duration were included. Statistical analysis involved calculating differences between pre- and post-treatment measurements for the various cardiovascular parameters divided by the pooled standard deviation. Further, we assessed the percentage of clinically relevant increased BP or HR, or documented arrhythmias.

Results: Eighteen clinical trials met the inclusion criteria (10 for MPH, 5 for AMP, and 7 for ATX) with data from 5837 participants (80.7% boys) and average duration of 28.7 weeks (range 4-96 weeks). All three medications were associated with a small, but statistically significant pre-post increase of SBP (MPH: standard mean difference [SMD] 0.25, 95% confidence interval [CI] 0.08-0.42, $p < 0.01$; AMP: SMD 0.09, 95% CI 0.03-0.15, $p < 0.01$; ATX: SMD 0.16, 95% CI 0.04-0.27, $p = 0.01$). MPH did not have a pre-post effect on DBP and HR. AMP treatment was associated with a small but statistically significant pre-post increase of DBP (SMD 0.16, CI 0.03-0.29, $p = 0.02$), as was ATX treatment (SMD 0.22, CI 0.10-0.34, $p < 0.01$). AMP and ATX were associated with a small to medium statistically significant pre-post increase of HR (AMP: SMD 0.37, CI 0.13-0.60, $p < 0.01$; ATX: SMD 0.43, CI 0.26-0.60, $p < 0.01$). The head-to-head comparison of the three medications did not reveal significant differences. Sensitivity analyses revealed that AMP studies of <18 weeks reported higher effect sizes on DBP compared with longer duration studies ($F(1) = 19.55$, $p = 0.05$). Further, MPH studies published before 2007 reported higher effect sizes on SBP than studies after 2007 ($F(1) = 5.346$, $p = 0.05$). There was no effect of the following moderators: type of medication, doses, sample size, age, gender, type of ADHD, comorbidity or dropout rate. Participants on medication reported 737 (12.6%) other cardiovascular effects. Notably, 2% of patients discontinued their medication treatment due to any cardiovascular effect. However, in the majority of patients, the cardiovascular effects resolved spontaneously, medication doses were changed or the effects were not considered clinically relevant. There were no statistically significant differences between the medication treatments in terms of the severity of cardiovascular effects.

Conclusions: Statistically significant pre–post increases of SBP, DBP and HR were associated with AMP and ATX treatment in children and adolescents with ADHD, while MPH treatment had a statistically significant effect only on SBP in these patients. These increases may be clinically significant for a significant minority

of individuals that experience larger increases. Since increased BP and HR in general are considered risk factors for cardiovascular morbidity and mortality during adult life, paediatric patients using ADHD medication should be monitored closely and regularly for HR and BP

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Complement Ther Med. 2016 Dec;29:56-62.

A SYSTEMATIC REVIEW OF THE AYURVEDIC MEDICINAL HERB BACOPA MONNIERI IN CHILD AND ADOLESCENT POPULATIONS.

Kean JD, Downey LA, Stough C.

OBJECTIVES: Clinicians utilise critical research to advance their knowledge when prescribing standard and alternative therapies for developmental disorders. Recent research has reported that the traditional Ayurvedic medicine Bacopa monnieri may improve cognitive outcomes in adult populations; however, few studies have investigated its benefits in younger cohorts. The aim of the current review is to systematically assess and critically summarize clinical trial outcomes and safety of Bacopa and its effects on the cognition and behaviour in children and adolescents.

METHOD: PubMed, Scopus, Cochrane Library, Google and CINAHL were searched up to August 2015 for trials investigating Bacopa monnieri in child and adolescent populations. There were no restrictions in study design. Cognitive and behavioural outcomes were grouped into validated constructs and effect sizes were calculated for all significant data to allow for direct comparisons.

RESULTS: Five studies met inclusion criteria for this review. The results demonstrated significant consistent improvements in the language behaviour cognitive domain and in a number of the memory sub-domains. Significant improvements were also seen in hyperactivity and attention-deficit domains. Overall outcome data demonstrated small to medium effect sizes (mean d=0.42). Safety and tolerability data was well reported for 80% of studies with only 2.3% of all participants reporting mild side-effects.

CONCLUSION: This review highlights the safe use of Bacopa monnieri in child and adolescent populations for improving elements of cognition as well as behaviour and attention-deficit domains. However, there is a significant need for replicated study designs and stringent statistical analysis to validate these outcomes

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Compr Psychiatry. 2016 Jul;68:56-59.

NEW DSM-5 CRITERIA FOR A.

Rigler T, Manor I, Kalansky A, et al.

OBJECTIVE: The new Diagnostic Statistical Manual (DSM) requires the presence of fewer symptoms to make a diagnosis of adult ADHD while the criteria for diagnosis in childhood are unchanged as compared to previous editions. This study examines the prevalence of adults meeting the revised DSM-5 symptoms cutoff as compared to the previous DSM-IV symptoms cutoff.

METHOD: This study is part of a larger nationwide study that evaluated the use of, and the attitudes toward, ADHD medications by university students. 445 students from four major university faculties were surveyed and filled out questionnaires for our study.

RESULTS: The proportion of participants that met the minimum threshold of six out of nine current symptoms in either of the two DSM-IV symptom domains (inattentive presentation and hyperactive/impulsive presentation) for ADHD was 12.7% while the proportion that met the minimum threshold of five symptoms in either of the DSM-5 symptom domains was 21%.

CONCLUSION: Since the new DSM requires fewer current symptoms for a diagnosis of ADHD, a significant increase (65%) was observed in the number of participants meeting the new cutoff as compared to the old DSM-IV symptoms cutoff. This increase in the number of adults meeting symptoms cutoff may affect the rates of adults diagnosed with ADHD. Using the new criteria may identify more adults with ADHD and fewer diagnoses will be missed. However, meeting the new symptoms cutoff should be considered within the overall clinical context to prevent over-diagnosis

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Deutsches Arzteblatt International. 2017;114:141-48.

ADHD IN GERMANY: TRENDS IN DIAGNOSIS AND PHARMACOTHERAPY-A COUNTRY-WIDE ANALYSIS OF HEALTH INSURANCE DATA ON ATTENTION-DEFICIT/ HYPERACTIVITY DISORDER (ADHD) IN CHILDREN, ADOLESCENTS AND ADULTS FROM 2009-2014.

Bachmann CJ, Philipsen A, Hoffmann F.

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Dev Neurorehabil. 2017 Feb;20:59-67.

EXPERIENCES OF FACILITATORS OR BARRIERS IN DRIVING EDUCATION FROM LEARNER AND NOVICE DRIVERS WITH ADHD OR ASD AND THEIR DRIVING INSTRUCTORS.

Almberg M, Selander H, Falkmer M, et al.

BACKGROUND: Little is known about whether individuals with autism spectrum disorder (ASD) or attention deficit hyperactive disorder (ADHD) experience any specific facilitators or barriers to driving education.

OBJECTIVE: To explore the facilitators or barriers to driving education experienced by individuals with ASD or ADHD who obtained a learner's permit, from the perspective of the learner drivers and their driving instructors.

METHODS: Data were collected from 33 participants with ASD or ADHD, and nine of their driving instructors.

RESULTS: Participants with ASD required twice as many driving lessons and more on-road tests than those with ADHD. Participants with ADHD repeated the written tests more than those with ASD. Driving license theory was more challenging for individuals with ADHD, whilst individuals with ASD found translating theory into practice and adjusting to "unfamiliar" driving situations to be the greatest challenges.

CONCLUSION: Obtaining a driving license was associated with stressful training experience

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Drug Ther Bull. 2016 May;54:56-60.

GUANFACINE FOR ADHD IN CHILDREN AND ADOLESCENTS.

Anon.

Prolonged-action guanfacine (Intuniv-Shire Pharmaceuticals Ltd) is a non-stimulant drug that has recently been licensed in Europe for the management of attention deficit hyperactivity disorder (ADHD) in children and adolescents aged 6-17 years for whom stimulants are unsuitable.(1) The company suggests that it has a unique mechanism of action in ADHD, providing improvement in core symptoms within 3 weeks with once-daily flexible dosing.(2) Here we review the evidence on the efficacy and safety of guanfacine in ADHD and consider whether it offers any advantages over other therapeutic options

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East Asian Arch Psychiatry. 2016 Dec;26:148-53.

CO-MORBIDITY IN ATTENTION-DEFICIT HYPERACTIVITY DISORDER: A CLINICAL STUDY FROM INDIA.

Jacob P, Srinath S, Girimaji S, et al.

OBJECTIVE: To assess the prevalence of neurodevelopmental and psychiatric co-morbidities in children and adolescents diagnosed with attention-deficit hyperactivity disorder at a tertiary care child and adolescent psychiatry centre.

METHODS: A total of 63 children and adolescents who were diagnosed with attention-deficit hyperactivity disorder and fulfilled the inclusion criteria were comprehensively assessed for neurodevelopmental and psychiatric co-morbidities. The tools used included the Mini-International Neuropsychiatric Interview for Children and Adolescents, Attention Deficit Hyperactivity Disorder Rating Scale IV (ADHD-RS), Children's Global Assessment Scale, Clinical Global Impression Scale, Vineland Social Maturity Scale, and Childhood Autism Rating Scale.

RESULTS: All except 1 subject had neurodevelopmental and / or psychiatric disorder co-morbid with attention-deficit hyperactivity disorder; 66.7% had both neurodevelopmental and psychiatric disorders. Specific learning disability was the most common co-existing neurodevelopmental disorder and oppositional

defiant disorder was the most common psychiatric co-morbidity. The mean baseline ADHD-RS scores were significantly higher in the group with psychiatric co-morbidities, especially in the group with oppositional defiant disorder.
CONCLUSION: Co-morbidity is present at a very high frequency in clinic-referred children diagnosed with attention-deficit hyperactivity disorder. Psychiatric co-morbidity, specifically oppositional defiant disorder, has an impact on the severity of attention-deficit hyperactivity disorder. Co-morbidity needs to be explicitly looked for during evaluation and managed appropriately

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Eating Weight Disord. 2017;22:91-96.

RESTING METABOLIC RATE, PULMONARY FUNCTIONS, AND BODY COMPOSITION PARAMETERS IN CHILDREN WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER.

Alpaslan AH, et al.

PURPOSE: Several studies of school-aged children with attention deficit hyperactivity disorder (ADHD) have found a higher prevalence of overweight/obesity compared with the general population. However, the scientific literature contains insufficient evidence to establish clear conclusions on pulmonary functions, resting metabolic rate (RMR), and body composition in children with ADHD. This study therefore investigates the pulmonary functions tests (PFTs), RMR, and body composition parameters in children with ADHD and evaluates their quality of life.
METHODS: Forty children with ADHD and 40 healthy controls participated in the study. The children's parents completed Conners' parent rating scale (CPRS) and the pediatric quality of life (PedsQL), and their teachers completed Conners' Teacher rating scale (CTRS). The child participants also completed the PedsQL. RMR, PFTs, and body composition parameters were investigated.
RESULTS: No significant differences in age, gender, and socioeconomic level were found. All CPRS subscales, except anxiety and psychosomatic conditions, were significantly different ($p < 0.05$). According to the CTRS, inattentiveness, hyperactivity, and conduct problems were significantly higher in the ADHD group. The results showed that the ADHD group's quality of life is worse than the control group. Body mass index, body composition parameters, RMR, and PFTs were not statistically different between the children with ADHD and the healthy controls.
CONCLUSIONS: Further studies with complex designs are needed to confirm the results.Emot

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Behav Difficulties. 2017;1-18.

AMBIVALENT ATTITUDES ABOUT TEACHING CHILDREN WITH ATTENTION DEFICIT/HYPERACTIVITY DISORDER (ADHD).

Anderson DL, Watt SE, Shanley DC

Drawing on attitude theories from social psychology, we conducted a survey of Australian pre-service (*n* = 327) and in-service (*n* = 127) teachers' attitudes about teaching children with attention-deficit/hyperactivity disorder (ADHD). This paper reports a content analysis of beliefs, affect and behaviours towards teaching children with ADHD and quantitative analyses pertaining to attitudinal ambivalence – that is, where a teacher may simultaneously report negative and positive evaluations of teaching children with ADHD. While on average, overall or global attitudes were mildly positive for both cohorts, considerable ambivalence about teaching children with ADHD was commonly experienced. Participants reported ambivalent beliefs, affect and behaviours, as well as ambivalence between these attitude components. Paradoxically, participants who knew more about ADHD and held stronger positive global attitudes about teaching children with ADHD reported less ambivalent behaviours towards these children, but reported more ambivalent beliefs. The implications for teachers' professional development and training are discussed

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Eur Arch Psychiatry Clin Neurosci. 2017 Apr;267:267-76.

A RANDOMIZED CONTROLLED TRIAL REPORTING FUNCTIONAL OUTCOMES OF COGNITIVE-BEHAVIOURAL THERAPY IN MEDICATION-TREATED ADULTS WITH ADHD AND COMORBID PSYCHOPATHOLOGY.

Young S, Emilsson B, Sigurdsson JF, et al.

Studies assessing psychological treatment of attention deficit hyperactivity disorder (ADHD) in adults are increasingly reported. However, functional outcomes are often neglected in favour of symptom outcomes. We investigated functional outcomes in 95 adults with ADHD who were already treated with medication and randomized to receive treatment as usual (TAU/MED) or psychological treatment (CBT/MED) using a cognitive-behavioural programme, R&R2ADHD, which employs both group and individual modalities. RATE-S functional outcomes associated with ADHD symptoms, social functioning, emotional control and antisocial behaviour were given at baseline, end of treatment and three-month follow-up. The Total composite score of these scales is associated with life satisfaction. In addition, independent evaluator ratings of clinicians who were blind to treatment arm were obtained on the Clinical Global Impression scale at each time point. CBT/MED showed overall (combined outcome at end of treatment and 3-month follow-up) significantly greater functional improvement on all scales. Post-group treatment effects were maintained at follow-up with the exception of emotional control and the Total composite scales, which continued to improve. The largest treatment effect was for the RATE-S Total composite scale, associated with life satisfaction. CGI significantly correlated with all outcomes except for social functioning scale at follow-up. The study provides further evidence for the effectiveness of R&R2ADHD and demonstrates the importance of measuring functional outcomes. The key mechanism associated with improved functional outcomes is likely to be behavioural control

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Eur Child Adolesc Psychiatry. 2017 Jan;26:123-36.

PRESCHOOL HYPERACTIVITY SPECIFICALLY ELEVATES LONG-TERM MENTAL HEALTH RISKS MORE STRONGLY IN MALES THAN FEMALES: A PROSPECTIVE LONGITUDINAL STUDY THROUGH TO YOUNG ADULTHOOD.

Smith E, Meyer BJ, Koerting J, et al.

Evidence of continuities between preschool hyperactivity and adult mental health problems highlights the potential value of targeting early identification and intervention strategies. However, specific risk factors are currently unclear. This large-scale prospective longitudinal study aimed to identify which hyperactive preschoolers are at the greatest long-term risk of poor mental health. One hundred and seventy children (89 females) rated as hyperactive by their parents, and 88 non-hyperactive controls (48 females) were identified from a community sample of 4215 3-year-olds. Baseline data relating to behavioral/emotional problems and background characteristics were collected. Follow-up mental health and functional impairment outcomes were collected between 14 and 25 years of age. At age 3 years, males and females in the hyperactive group had similarly raised levels of hyperactivity and other behavior problems. In adolescence/young adulthood, these individuals showed elevated symptoms of ADHD, conduct disorder, mood disorder, anxiety and autism, as well as functional impairment. Preschool hyperactivity was strongly predictive of poor adolescent/adult outcomes for males across domains with effects being specifically driven by hyperactivity. For females, the effects of preschool hyperactivity were smaller and dropped to non-significant levels when other preschool problems were taken into account. Environmental risk factors also differed between the sexes, although these may also have been mediated by genetic risk. In conclusion, these results demonstrate marked sex differences in preschool predictors of later adolescent/adult mental health problems. Future research should include a measure of preschool inattention as well as hyperactivity. The findings highlight the potential value of tailored approaches to early identification strategies

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Eur Child Adolesc Psychiatry. 2017 Mar;26:303-13.

SEROTONIN TRANSPORTER POLYMORPHISM MODERATES THE EFFECTS OF CAREGIVER INTRUSIVENESS ON ADHD SYMPTOMS AMONG INSTITUTIONALIZED PRESCHOOLERS.

Baptista J, Belsky J, Mesquita A, et al.

Research consistently chronicles a variety of mental health difficulties that plague institutionally reared children, including attention-deficit/hyperactivity disorder (ADHD), even if not all institutionalized children evince such problems. In seeking to extend work in this area, this research on gene x environment (GXE) interplay investigated whether the effect of the quality of institutional care-most notably, caregiver intrusiveness-on ADHD symptoms is moderated by the serotonin transporter (5-HTTLPR) polymorphism. One hundred and twenty-seven institutionalized preschoolers were evaluated using the Child Behavior Checklist. Caregiver-rated attention problems and hyperactivity were unrelated to both 5-HTTLPR polymorphism and caregiver intrusiveness. A significant GXE effect, independent of age at placement or duration of institutionalization, emerged, however, consistent with the differential-susceptibility hypothesis: s/s homozygotes manifest the most and least ADHD symptoms when they experienced, respectively, more and less intrusive caregiving. These results provide new insight into the reasons why some institutionalized children, but not others, exhibit ADHD symptoms

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Eur Child Adolesc Psychiatry. 2017 Mar;26:281-91.

STRUCTURE AND CLINICAL CORRELATES OF OBSESSIVE-COMPULSIVE SYMPTOMS IN A LARGE SAMPLE OF CHILDREN AND ADOLESCENTS: A FACTOR ANALYTIC STUDY ACROSS FIVE NATIONS.

Hojgaard DR, Mortensen EL, Ivarsson T, et al.

The underlying structure of obsessive-compulsive disorder (OCD) remains to be confirmed in child and adolescent populations. In this paper we report the first factor analytic study of individual OCD items from Children's Yale-Brown Obsessive Compulsive Scale (CY-BOCS). OCD symptoms were assessed using the CY-BOCS symptom checklist in a sample of 854 patients with OCD (7-18 years of age) recruited from clinics in five countries. Pooled data were subjected to exploratory and confirmatory factor analysis (CFA) to identify the optimal factor structure. Various models were tested for age and gender subgroups. Also, the invariance of the solution across age and gender was tested and associations with demographic and clinical factors were explored. A three-factor model provided the best-fit solution. It consisted of the following factors: (1) harm/sexual, (2) symmetry/hoarding, (3) contamination/cleaning. The factor structure was invariant for age and gender across subgroups. Factor one was significantly correlated with anxiety, and factor two with depression and anxiety. Factor three was negatively correlated with tic disorder and attention-deficit/hyperactivity disorder (ADHD). Females had higher scores on factor two than males. The OCD symptom structure in children and adolescents is consistent across age and gender and similar to results from recent child and adolescents although hoarding may not be a separate factor. Our three-factor structure is almost identical to that seen in early studies on adults. Common mental disorders had specific patterns of associations with the different factors

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Eur Child Adolesc Psychiatry. 2017 Feb;26:253-62.

MATERNAL PSYCHOPATHOLOGY AND OFFSPRING CLINICAL OUTCOME: A FOURâ€'YEAR FOLLOWâ€'UP OF BOYS WITH ADHD.

Agha SS, Zammit S, Thapar A, et al.

Previous cross-sectional research has shown that parents of children with attention deficit hyperactivity disorder (ADHD) have high rates of psychopathology, especially ADHD and depression. However, it is not clear whether different types of parent psychopathology contribute to the course and persistence of ADHD in the child over time. The aim of this two wave study was to investigate if mother self-reported ADHD and depression influence persistence of offspring ADHD and conduct disorder symptom severity in adolescents diagnosed with ADHD in childhood. A sample of 143 males with a confirmed diagnosis of ADHD participated in this study. ADHD and conduct disorder symptoms were assessed at baseline and reassessed 4 years

later. The boys in this sample had a mean age of 10.7 years at Time 1 (SD 2.14, range 6â€“15 years) and 13.73 years at Time 2 (SD 1.74, range 10â€“17 years). Questionnaire measures were used to assess ADHD and depression symptoms in mothers at Time 1. Mother self-reported ADHD was not associated with a change in child ADHD or conduct symptom severity over time. Mother self-reported depression was found to predict an increase in child conduct disorder symptoms, but did not contribute to ADHD symptom levels. This study provides the first evidence that concurrent depression in mothers may be a predictor of worsening conduct disorder symptoms in adolescents with ADHD. It may, therefore, be important to screen for depression in mothers of children with ADHD in clinical practice to tailor interventions accordingly.

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Eur Child Adolesc Psychiatry. 2017;1-23.

COMPARATIVE EFFICACY AND SAFETY OF ATTENTION-DEFICIT/HYPERACTIVITY DISORDER PHARMACOTHERAPIES, INCLUDING GUANFACINE EXTENDED RELEASE: A MIXED TREATMENT COMPARISON.

Joseph A, Ayyagari R, Xie M, et al.

This study compared the clinical efficacy and safety of attention-deficit/hyperactivity disorder (ADHD) pharmacotherapy in children and adolescents 6-17 years of age. A systematic literature review was conducted to identify randomized controlled trials (RCTs) of pharmacologic monotherapies among children and adolescents with ADHD. A Bayesian network meta-analysis was conducted to compare change in symptoms using the ADHD Rating Scale Version IV (ADHD-RS-IV), Clinical Global Impression-Improvement (CGI-I) response, all-cause discontinuation, and adverse event-related discontinuation. Thirty-six RCTs were included in the analysis. The mean (95% credible interval [CrI]) ADHD-RS-IV total score change from baseline (active minus placebo) was -14.98 (-17.14, -12.80) for lisdexamfetamine dimesylate (LDX), -9.33 (-11.63, -7.04) for methylphenidate (MPH) extended release, -8.68 (-10.63, -6.72) for guanfacine extended release (GXR), and -6.88 (-8.22, -5.49) for atomoxetine (ATX); data were unavailable for MPH immediate release. The relative risk (95% CrI) for CGI-I response (active versus placebo) was 2.56 (2.21, 2.91) for LDX, 2.13 (1.70, 2.54) for MPH extended release, 1.94 (1.59, 2.29) for GXR, 1.77 (1.31, 2.26) for ATX, and 1.62 (1.05, 2.17) for MPH immediate release. Among non-stimulant pharmacotherapies, GXR was more effective than ATX when comparing ADHD-RS-IV total score change (with a posterior probability of 93.91%) and CGI-I response (posterior probability 76.13%). This study found that LDX had greater efficacy than GXR, ATX, and MPH in the treatment of children and adolescents with ADHD. GXR had a high posterior probability of being more efficacious than ATX, although their CrIs overlapped.

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Eur Child Adolesc Psychiatry. 2017;1-11.

FURTHER EVIDENCE FOR THE ROLE OF PREGNANCY-INDUCED HYPERTENSION AND OTHER EARLY LIFE INFLUENCES IN THE DEVELOPMENT OF ADHD: RESULTS FROM THE IDEFICS STUDY.

Pohlabeln H, Rach S, de Henauw S, et al.

The aim of this study is to investigate whether in addition to established early risk factors other, less studied pre-, peri-, and postnatal influences, like gestational hypertension or neonatal respiratory disorders and infections, may increase a childΓÇÖs risk of developing attention-deficit/hyperactivity disorders (ADHD). In the IDEFICS study more than 18,000 children, aged 2–11.9 years, underwent extensive medical examinations supplemented by parental questionnaires on pregnancy and early childhood. The present analyses are restricted to children whose parents also completed a supplementary medical questionnaire (n = 15,577), including the question whether or not the child was ever diagnosed with ADHD. Multilevel multivariable logistic regression was used to assess the association between early life influences and the risk of ADHD. Our study confirms the well-known association between maternal smoking during pregnancy and a childΓÇÖs risk of ADHD. In addition, our study showed that children born to mothers younger than 20 years old were 3–4 times more likely to develop ADHD as compared to children born to mothers aged 25 years and older. Moreover, we found that children whose mothers suffered from pregnancy-induced hypertension had an approximately twofold risk of ADHD (OR 1.95; 95% CI 1.09–3.48). This also holds true for infections during the first 4 weeks after birth (OR 2.06; 95% CI 1.05–4.04). In addition, although not

statistically significant, we observed a noticeable elevated risk estimate for neonatal respiratory disorders (OR 1.76; 95% CI 0.91–3.41). Hence, we recommend that these less often studied pre-, peri, and postnatal influences should get more attention when considering early indicators or predictors for ADHD in children. However, special study designs such as genetically sensitive designs may be needed to derive causal conclusions

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Eur Child Adolesc Psychiatry. 2017;1-10.

WHAT MOTIVATES INDIVIDUALS WITH ADHD? A QUALITATIVE ANALYSIS FROM THE ADOLESCENT□ÇÖS POINT OF VIEW.

Morsink S, Sonuga-Barke E, Mies G, et al.

Individuals with ADHD appear to respond differently to incentives than their peers. This could be due to a general altered sensitivity to reinforcers. However, apart from differences in the degree of motivation, individuals with ADHD might also be motivated by qualitatively different factors. This study aimed to harvest a range of motivational factors and identify ADHD-related qualitative differences in motivation, from the adolescentΓÇÖs point of view. Semi-structured interviews allowing participants to describe what motivates them in daily life were conducted with young adolescents (9–16 years) with and without ADHD. Thematic analysis was undertaken using NVivo software. Major themes relating to motivation were identified from the interview data. These were: (1) achieving a sense of togetherness; (2) feeling competent; (3) fulfilling a need for variation; (4) gaining pleasure from applying effort to achieve a goal; (5) valuing social reinforcement; (6) desiring to be absorbed/forget problems; (7) feeling free and independent, (8) attaining material reinforcement; and (9) an enjoyment of bodily stimulation. The theme structure was very similar for both groups. However, individuals with ADHD differed in some specifics: their focus on the passing of time, the absence of preference for predictable and familiar tasks, and their less elaborate description of the togetherness theme. A broad range of motivational themes was identified, stretching beyond the current focus of ADHD research and motivational theories. Similarities and differences in motivational values of individuals with and without ADHD should be taken into account in reward sensitivity research, and in psychological treatment

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Eur Child Adolesc Psychiatry. 2017;1-10.

THE FASTER INTERNAL CLOCK IN ADHD IS RELATED TO LOWER PROCESSING SPEED: WISC-IV PROFILE ANALYSES AND TIME ESTIMATION TASKS FACILITATE THE DISTINCTION BETWEEN REAL ADHD AND PSEUDO-ADHD.

Walg M, Hapfelmeier G, El-Wahsch D, et al.

Alterations in temporal processing may represent a primary cause of key symptoms in ADHD. This study is aimed at investigating the nature of time-processing alterations in ADHD and assessing the possible utility of testing time estimation for clinical diagnostics. Retrospective verbal time estimation in the range of several minutes was examined in 50 boys with ADHD and 53 boys with other mental disorders. All participants (age 7-16) attended an outpatient clinic for ADHD diagnostics. The diagnostic assessment included the WISC-IV. Subjects with ADHD made longer and less accurate duration estimates than the clinical control group. The ADHD group showed a specific WISC-IV profile with processing speed deficits. In the ADHD group there was a correlation between processing speed and quality of time estimation that was not observed in the comparison group: higher processing speed indices were related to more accurate duration estimates. The findings provide support for the presence of a faster internal clock in subjects with ADHD and lend further support to the existence of a specific WISC-IV profile in subjects with ADHD. The results show that analyzing WISC-IV profiles and time estimation tasks are useful differential diagnosis tools, particularly when it comes to distinguishing between real ADHD- and pseudo-ADHD

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Eur J Paediatr Neurol. 2017.

CHARACTERISTICS OF SLEEP IN SOCIALLY VULNERABLE ADOLESCENTS.

Romanzini LP, dos Santos A, Nunes ML.

Importance: This study may help understand the effects of an unfavorable environment in sleep quality of adolescents.

Objective: To investigate sleep quality in socially vulnerable adolescents, correlating the results with cognitive problems and attention deficit/hyperactivity disorder, and assessing the effectiveness of sleep hygiene and an educational intervention. Design: Cross-sectional and interventional study.

Setting: an educational charitable center supported by a Catholic institution, in Porto Alegre, southern Brazil.

Participants: 125 male and female high school students. Interventions: As first step the subjects were administered specific questionnaires, the Pittsburgh Sleep Quality Index (PSQI) and the Epworth Sleepiness Scale (ESS), followed by an educational activity that was combined with an unblinded, randomized interventional study. Next, a cross-sectional study was conducted to determine the influence of cognition and ADHD on the sleep. Main outcome and measures: Sleep was evaluated using PSQI and ESS. Cognitive assessment was based on the Wechsler Abbreviated Scale of Intelligence and ADHD by a clinical interview the Multimodal Treatment Study for ADHD (MTA-SNAP-IV).

Results: The average duration of sleep per night were 6 h 30 m. 80% of the sample presented sleep complains. Of these, 44% had excessive daytime sleepiness and 69.6% had poor sleep quality related to use of electronic media, environmental violence, and emotional issues. There were no significant associations between sleep problems and cognitive problems or ADHD. Sleep quality improved in 17% of the 53 students with previous sleep complains who participated in any of the two interventions.

Conclusions: A high prevalence of sleep deprivation and sleep complains was found in the study sample. The interventions showed some positive effects on the improvement of sleep quality

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Eur Neuropsychopharmacol. 2017.

TRENDS IN ADHD MEDICATION USE IN CHILDREN AND ADOLESCENTSIN FIVE WESTERNCOUNTRIES, 2005-2012.

Bachmann CJ, Wijlaars LP, Kalverdijk LJ, et al.

Over the last two decades, the use of ADHD medication in US youth has markedly increased. However, less is known about ADHD medication use among European children and adolescents. A repeated cross-sectional design was applied to national or regional data extracts from Denmark, Germany, the Netherlands, the United Kingdom(UK) and the United States(US) for calendar years 2005/2006-2012. The prevalence of ADHD medication use was assessed, stratified by age and sex. Further more, the most commonly prescribed ADHD medications were assessed. ADHD medication use prevalence increased from 1.8% to 3.9% in the Netherlands cohort (relative increase: +111.9%), from 3.3% to 3.7% in the UScohort (+10.7%), from 1.3%to 2.2% in the German cohort(+62.4%), from 0.4% to 1.5% in the Danish cohort (+302.7%), and from 0.3% to 0.5% in the UK cohort (+56.6%). ADHD medication use was highest in 10-14-year olds, peaking in the Netherlands (7.1%) and the US(8.8%). Methylphenidate use predominated in Europe, whereas in the US amphetamines were nearly as common as methylphenidate. Although there was a substantially greater use of ADHD medications in the US cohort, there was a relatively greater increase in ADHD medication use in youth in the four Europe an countries. ADHD medication use patterns in the US differed markedly from those in western European countries

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Exp Brain Res. 2017;1-10.

REM THETA ACTIVITY ENHANCES INHIBITORY CONTROL IN TYPICALLY DEVELOPING CHILDREN BUT NOT CHILDREN WITH ADHD SYMPTOMS.

Cremone A, Lugo-Candelas CI, Harvey EA, et al.

Sleep disturbances impair cognitive functioning in typically developing populations. Children with attention-deficit/hyperactivity disorder (ADHD), a disorder characterized by impaired inhibitory control and attention, commonly experience sleep disturbances. Whether inhibitory impairments are related to sleep deficits in

children with ADHD is unknown. Children with ADHD (n = 18; Mage = 6.70 years) and typically developing controls (n = 15; Mage = 6.73 years) completed a Go/No-Go task to measure inhibitory control and sustained attention before and after polysomnography-monitored overnight sleep. Inhibitory control and sustained attention were improved following overnight sleep in typically developing children. Moreover, morning inhibitory control was positively correlated with rapid eye movement (REM) theta activity in this group. Although REM theta activity was greater in children with ADHD compared to typically developing children, it was functionally insignificant. Neither inhibitory control nor sustained attention was improved following overnight sleep in children with ADHD symptoms, and neither of these behaviors was associated with REM theta activity in this group. Taken together, these results indicate that elevated REM theta activity may be functionally related to ADHD symptomology, possibly reflecting delayed cortical maturation

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Expert Opin Ther Pat. 2016 Jul;26:799-814.

TREATMENTS AND COMPOSITIONS FOR ATTENTION DEFICIT HYPERACTIVITY DISORDER: A PATENT REVIEW.

Molina-Carballo A, Checa-Ros A, Munoz-Hoyos A.

INTRODUCTION: Attention deficit and hyperactivity disorder (ADHD) is a syndrome that affects children prior to 12 years of age. ADHD manifests as inappropriate behavior and learning difficulties and, in many cases, it persists into adulthood. In most cases, pharmacological treatment is sufficient; however, this approach frequently does not address all symptomatology of comorbidities and also affects the risk of secondary side effects that may influence compliance.

AREAS COVERED: This review emphasizes the recent progress in ADHD treatment, which was published in the patent literature from 2005-2015. We focused on novel mechanisms of action and potential treatments for achieving control of ADHD comorbidities, offering theoretical advantages compared with current medication. Newer agents are also proposed in recent patents and compounds for child and adult ADHD.

EXPERT OPINION: The patented drugs and compositions may provide a greater opportunity to develop more personalized, effective, and tolerable medications, without the liability of abuse. Particularly interesting will be the results obtained with drugs with a dual mechanism of action, agonists of trace amine receptors, and compounds that exhibit cognitive enhancing properties. Effectiveness and efficacy studies are also necessary to determine whether the characteristics of different drugs are related to their effects on disease

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Front Psychiatry. 2017;8.

TEMPORAL ASSOCIATION OF CERTAIN NEUROPSYCHIATRIC DISORDERS FOLLOWING VACCINATION OF CHILDREN AND ADOLESCENTS: A PILOT CASE-CONTROL STUDY.

Leslie DL, Kobre RA, Richmand BJ, et al.

Background: Although the association of the measles, mumps, and rubella vaccine with autism spectrum disorder has been convincingly disproven, the onset of certain brain-related autoimmune and inflammatory disorders has been found to be temporally associated with the antecedent administration of various vaccines. This study examines whether antecedent vaccinations are associated with increased incidence of obsessive-compulsive disorder (OCD), anorexia nervosa (AN), anxiety disorder, chronic tic disorder, attention deficit hyperactivity disorder, major depressive disorder, and bipolar disorder in a national sample of privately insured children.

Methods: Using claims data, we compared the prior year's occurrence of vaccinations in children and adolescents aged 6-15 years with the above neuropsychiatric disorders that were newly diagnosed between January 2002 and December 2007, as well as two control conditions, broken bones and open wounds. Subjects were matched with controls according to age, gender, geographical area, and seasonality. Conditional logistic regression models were used to determine the association of prior vaccinations with each condition.

Results: Subjects with newly diagnosed AN were more likely than controls to have had any vaccination in the previous 3 months [hazard ratio (HR) 1.80, 95% confidence interval 1.21-2.68]. Influenza vaccinations during the prior 3, 6, and 12 months were also associated with incident diagnoses of AN, OCD, and an

anxiety disorder. Several other associations were also significant with HRs greater than 1.40 (hepatitis A with OCD and AN; hepatitis B with AN; and meningitis with AN and chronic tic disorder).
Conclusion: This pilot epidemiologic analysis implies that the onset of some neuropsychiatric disorders may be temporally related to prior vaccinations in a subset of individuals. These findings warrant further investigation, but do not prove a causal role of antecedent infections or vaccinations in the pathoetiology of these conditions. Given the modest magnitude of these findings in contrast to the clear public health benefits of the timely administration of vaccines in preventing mortality and morbidity in childhood infectious diseases, we encourage families to maintain vaccination schedules according to CDC guidelines

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Front Psychol. 2017 Jan;8.

GAIT IN CHILDREN WITH ATTENTION-DEFICIT HYPERACTIVITY DISORDER IN A DUAL-TASK PARADIGM.

Manicolo O, Grob A, Hagmann-von Arx P.

The aim was to examine gait in school-aged children with attention-deficit hyperactivity disorder (ADHD) and typically developing controls in a dual-task paradigm. Thirty children with ADHD (without or off medication) aged 7-13 years and 28 controls walked without an additional task (single-task walking) and while performing a concurrent cognitive or motor task (dual-task walking). Gait was assessed using GAITRite recordings of spatiotemporal and variability gait parameters. Compared to single-task walking, dual-tasking significantly altered walking performance of children with and without ADHD, whereby dual-task effects on gait were not different between the two groups. For both children with ADHD and controls the motor concurrent task had a stronger effect on gait than the cognitive concurrent task. Gait in children with and without ADHD is affected in a dual-task paradigm indicating that walking requires executive functions. Future investigations of children's dual-task walking should account for the type of concurrent tasks

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Front Psychol. 2017 Jan;8.

IMPAIRED MEMORY FOR INSTRUCTIONS IN CHILDREN WITH ATTENTION-DEFICIT HYPERACTIVITY DISORDER IS IMPROVED BY ACTION AT PRESENTATION AND RECALL.

Yang Tx, Allen RJ, Holmes J, et al.

Children with attention deficit hyperactivity disorder (ADHD) often fail to comply with teacher instructions in the classroom. Using action during presentation or recall can enhance typically developing children's abilities to complete multi-step instruction sequences. In this study, we tested the ability to following instructions in children with ADHD under different conditions to explore whether they show the same beneficial effects of action. A total of 24 children with ADHD and 27 typically developing children either listened to or viewed demonstrations of instructions during encoding, and then either verbally repeated or physically performed the sequences during recall. This resulted in four conditions: spoken-verbal, spoken-enacted, demonstration-verbal, and demonstration-enacted. Children with ADHD were significantly impaired in all conditions of the following instructions task relative to the typically developing group. Both groups showed an enacted-recall advantage, with superior recall by physical performance than oral repetition. Both groups also benefitted from demonstration over spoken presentation, but only when the instructions were recalled verbally. These findings suggest that children with ADHD struggle to complete multi-step instructions, but that they benefit from action-based presentation and recall in the same way as typically developing children. These findings have important implications for educators, suggesting that motor-based methods of instruction-delivery might enhance classroom learning both for children with and without developmental disorders.

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Galen Medical Journal. 2016;5:188-93.

ASSESSMENT OF TOXOPLASMA SEROPOSITIVITY IN CHILDREN SUFFERING FROM ATTENTION DEFICIT HYPERACTIVITY DISORDER.

Afsharpaiman S, Khosravi MH, Faridchehr M, et al.

Background: Toxoplasmosis, a protozoan infection caused by Toxoplasma gondii, is suggested to be a risk factor for many psychological disorders such as schizophrenia and depression. Attention deficit hyperactivity disorder (ADHD) is one of the most common psychiatric disorders among children. Previous studies have assessed the correlation between ADHD and infectious diseases like toxoplasmosis. So we aimed to investigate the possible correlation between Toxoplasma seropositivity and ADHD in children. Materials and **Methods**: In this cross-sectional study children with signs of ADHD were regarded as patients and underwent clinical assessments. Diagnosis of these patients was based on DSM-IV-TR system which was performed by a pediatric psychiatrist. Forty-eight Children without signs of ADHD or other psychic disorders were considered as control, and 48 patients were considered as case group. Parents were asked to answer a questionnaire including demographic, pregnancy and habitual questions. Blood samples were taken from all individuals and assessed for anti-Toxoplasma IgM and IgG antibodies.

Results: Ninety-six male and female patients with a mean age of 8.12 years underwent analysis. Seropositivity rate for anti-T.gondii IgG antibody was 4.2% in the case and 2.1% in control individuals (P=0.92). Anti-T.gondii IgM antibodies were not found in control individuals while it was found in 2.1% of case individuals (P=0.74). There was no statistically significant association between seroprevalence of IgM (P=0.74) and IgG (P=0.92) antibodies and ADHD in study individuals.

Conclusion: Our findings showed that the toxoplasmosis seropositivity has no significant difference between children with and without ADHD. Further studies are needed with a larger amount of individuals

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Genet Couns. 2016;27:295-303.

PARTIAL TRISOMY 5P12-Q11.2 RESULTING FROM A MARKER CHROMOSOME: A NEW CASE REPORT WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER.

Erdem HB, Sahin I, Tasdemir S, et al.

Partial trisomy of chromosome 5 was first described by Lejeune et al. in 1964 on the short arm (12). The vast majority of the partial trisomy 5 cases include 5p duplications; however we reported a small supernumerary marker chromosome. General symptoms include developmental delay, mental retardation, seizures, respiratory difficulties, congenital heart defects, abdominal muscle hypoplasia and dysmorphic features such as macrocephaly, enlarged anterior fontanelle, dolichocephaly, upslanting palpebral fissures, epicanthal folds, hypertelorism, abnormal ears, midface hypoplasia, short nose, broad nasal bridge and microretrognathia. Arachnodactyly and club foot may be seen as cytoskeletal abnormalities and, hypotonia may be determined in neurological exam. Here we reported a case with developmental delay, attention deficit hyperactivity disorder, mild mental retardation and dysmorphic features, caused by a new small supernumerary marker chromosome, generating partial trisomy 5pl2-ql 1.2. To our knowledge, this small supernumerary marker chromosome has not been reported before. Severe type of partial trisomy 5 includes seizures, congenital heart defects, hypotonia and failure to thrive. Previously reported partial trisomy 5 cases, who showed severe phenotype, had usually duplicated 5pl3 region. Therefore, patients, who do not have duplicated 5pl3, showed mild phenotype. Also, duplication of the long arm of chromosome 5, may contribute to the milder phenotype and the longer survival in partial trisomy 5 patients. Attention deficit hyperactivity disorder, which we described in the present case, may be a result of partial trisomy 5, because it includes ADHD4 gene. This case may help better understanding the karyotype/phenotype correlation related to partial trisomy 5

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Harv Rev Psychiatry. 2017;25:50-64.

PHARMACOLOGICAL TREATMENT OF ADHD IN ADDICTED PATIENTS: WHAT DOES THE LITERATURE TELL US?

Carpentier PJ, Levin FR.

LEARNING OBJECTIVES: After participating in this activity, learners should be better able to:• Evaluate pharmacologic treatment of attention deficit/hyperactivity disorder (ADHD) in patients with substance use disorder (SUD) • Assess the causes of the diminished efficacy of ADHD medication in patients with comorbid SUD OBJECTIVE: Substance use disorder (SUD) and attention-deficit/hyperactivity disorder (ADHD) frequently co-occur, and the presence of ADHD complicates the treatment of the addiction. Pharmacotherapy is a potent intervention in childhood and adult ADHD, but findings have been mixed in adolescent and adult ADHD patients with SUDs. This review focuses on several contributing factors and possible explanations, with implications both for future research and for clinical practice.

METHOD: This systematic review examined all randomized, placebo-controlled trials of pharmacotherapy for ADHD in adult and adolescent SUD patients.

RESULTS: The number of studies is limited, and several studies are hampered by qualitative flaws. The results, in general, are inconclusive for most medications studied, but more recent trials using psychostimulants in robust dosing have demonstrated significantly positive results.

CONCLUSION: In reviewing these trials, possible explanations relating to the particular characteristics and problems of this complex patient group are discussed. Several factors, including ADHD symptom severity, psychiatric comorbidity, persistent drug use, choice of medication, and concomitant psychosocial intervention, influence study results. Taking these factors into account may improve the likelihood of detecting significant effects in future research, as the recent positive trials have indicated, and may help in the appropriate selection of pharmacotherapy in clinical practice

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Int J Pediatr Otorhinolaryngol. 2017 Jan;92:103-07.

PSYCHOLOGICAL STATUS IN CHILDREN WITH EAR AND NOSE FOREIGN BODY INSERTION.

Bakhshaee M, Hebrani P, Shams M, et al .

OBJECTIVE: Children with psychological disorders are prone to various unintentional injuries, one of the most common of which is foreign body inserting. In spite of the high incidence, the association is not studied yet.

METHODS: This is a case control study in otorhinolaryngology and psychology departments, at a tertiary referral teaching hospital. One hundred five children (2-12 years old) who were referred for removal of foreign bodies in their ear or nose over a period of one year were selected for the study. Also, 155 children were selected and matched from the same community as the controls. Parents were given the standard strengths and difficulty questionnaire (SDQ) for psychological evaluation of their child. The total score and also the subscales for emotional symptoms, hyperactivity disorders, conduct problems, peer-relationship problemsand prosocialbehaviors were recorded and statistical analysis was performed.

RESULTS: In the case group, 34 cases (%32.4) were suffering from foreign bodies in their ear, 70 cases (%66.7) in their nose, and just one case (%1) in both. Age and sex distributionin the two groups were comparable. There were significant differences of SDQ scores between the two groups in total score ($p < 0.001$), emotional symptoms ($p < 0.001$), hyperactivity disorders ($p < 0.001$), conduct problems ($p < 0.001$), and prosocial behaviors ($p < 0.001$). However peer-relationship problems showed no significant difference between the two groups ($p = 0.161$).

CONCLUSION: Psychological problems are more common in children with foreign bodies than the controls. Thus physicians are recommended to consider referring these patients to the pediatric psychologist

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Int J Ment Health Addict. 2017 Feb;15:100-09.

NEUROFEEDBACK ASSOCIATED WITH NEUROCOGNITIVE-REHABILITATION TRAINING ON CHILDREN WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER (ADHD).

Pahlevanian A, Alirezaloo N, Naghel S, et al.

Neurofeedback is a computer-based behavior training gaining increasing interest in the treatment of children with attention-deficit hyperactivity disorder (ADHD), but is not a complete therapy for these patients. To meet the need for a more integrative approach, this study used neurofeedback with cognitive rehabilitation therapy as a more comprehensive approach for children with ADHD. Thirty children (females) were selected randomly from visitors of 5 clinics in Tehran city. Subjects were placed into 2 experimental groups and 1 control group. Groups were matched based on age, gender and socioeconomic status. One experimental group solely received neurofeedback in 10 sessions, the other experimental group received neurofeedback with cognitive rehabilitation therapy, and the control group left therapy received no therapy or left in the initial stages of therapy. Integrated visual and auditory test (IVA) was used pre-test and post-test to measure attention and impulsivity in children with ADHD, in addition to Neurocognitive Joyful Attentive Training Intervention (NEJATI). Data was analyzed using dependent T-test and analysis of covariance (ANCOVA). There are meaningful differences between all groups in attention and impulsivity factors. The group who received neurofeedback with cognitive rehabilitation therapy showed more improvement in attention and impulsivity factors compared to the group who received only neurofeedback and the control group with no treatment. There was also a significant difference between the solely neurofeedback group and control group in the attention factor. Neurofeedback is a facilitator therapy to improve the attention factor in children with ADHD, but is not a complete therapy due to its lack of support in performance factors. A complementary therapy such as cognitive rehabilitation therapy that focuses more on performance factors would be a more effective therapy as it leads to more positive effects on impulsivity and hyperactivity

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International Journal of Pharmacy Practice. 2015;23:31-32.

IDENTIFYING OPPORTUNITY AS THE BARRIER TO ADHD DRUG HOLIDAYS: APPLICATION OF THE BEHAVIOURAL CHANGE WHEEL.

Ibrahim K, Donyai P.

Background: Researchers have identified a variety of reasons for non-adherence to guidelines that include individual as well as organisational factors. For example, unfamiliarity with guidelines, lack of time / resources as well as disagreement with guidelines can act as barriers to implementing recommendations. The National Institute for Health and Care Excellence recommendations on the treatment of Attention Deficit Hyperactivity Disorder (ADHD) in children and adolescents, call for a review of medication at least annually. Although the impact of brief periods of no treatment must be taken into account as part of the review, 'drug holidays' (DH) are mainly recommended if growth has been suppressed by medication. However, locally, prescribers are asked to plan two-week DHs after two years of treatment to test continuing need for medication under shared-care arrangements, which our research shows is rarely practised [1]. The aim of this study was to identify the barriers to prescribers' engagement with planned DHs from ADHD medication by applying a behavioural change system [2].

Methods: The "COM-B system" was first used in order to identify barriers according to this framework's three components; capability, opportunity, and motivation. [2]. Health professionals involved in shared-care prescribing for children and adolescents with ADHD in Berkshire were included. Transcripts from interviews with GPs (n=8), (recruited from the NHS Berkshire cluster by posted letters and through the "snowball" technique), and secondary-care practitioners (n=8), (recruited via a child and adolescent psychiatrist collaborator) were analysed against 14 Theoretical Framework Domains that map onto the COM-B components. The behaviour change wheel, which includes the COM-B system as the hob, was then used in order to identity possible interventions or policies, for increasing prescribers' engagement with planned DHs, according to the component(s) in the COM-B system deemed to be relevant. This work was approved by the University of Reading Research Ethics Committee, local secondary- and primary-care R&D offices.

Results: Different barriers to prescribers' engagement with DHs from ADHD medication were identified. Capability, in terms of knowledge and physical and psychological skills was not a barrier for secondary-care practitioners but was for GPs needing more education and training about ADHD and worrying about possible

withdrawal effects. Opportunity was a main barrier for both GPs and secondary-care practitioners, who cited lack of time and unavailability of educational material for families, respectively. Motivation was more complex to define for both secondary-care practitioners and GPs, with the former accepting DHs on reflection and the latter being more accepting due to worries about long-term medication side-effects as well as cost savings. On mapping these barriers to the behaviour change wheel, 'enablement' was identified as a key activity targeting all three components, which could feasibly increase prescribers' engagement with planned DHs.
Conclusion: The application of the behavioural change wheel identified a number of key barriers to prescribers' engagement with DHs in children and adolescents with ADHD. Accordingly, 'enablement' was identified as a suitable behaviour change intervention. A possible example of an 'enablement' intervention is the creation of an educational and decision aid resource, which does not currently exist. References 1- Ibrahim, K., Masters, K., Donyai, P. (2014). Caught in the eye of the storm: explaining the lack of engagement with methylphenidate drug holidays in children with ADHD. International Journal of Pharmacy Practice, 22 (S1), p 2-27. 2- Michie, S., Van Stralen, M., & West, R. (2011). The behaviour change wheel: a new method for characterising and designing behaviour change interventions. Implementation Science, 6, 42
Publication insights: Identifying opportunity as the barrier to ADHD drug holidays: application of the behavioural change wheel.. Available from: https://www.researchgate.net/publication/275209459_Identifying_opportunity_as_the_barrier_to_ADHD_drug_holidays_application_of_the_behavioural_change_wheel [accessed Apr 7, 2017].

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Int J Psychiatry Clin Pract. 2017;1-6.

PSYCHOPATHOLOGICAL, TEMPERAMENTAL, AND CHARACTERISTIC FACTORS IN ADULTS WITH REMAINING CHILDHOOD ATTENTION-DEFICIT HYPERACTIVITY SYMPTOMS.

Kim KM, Nam S, Kim SY, et al.

OBJECTIVES: To investigate differences in psychopathological, temperamental and characteristic factors between young adults with and without persistent Attention-Deficit Hyperactivity disorder (ADHD) symptoms.
METHODS: A total of 429 university students were divided into three groups: persistent adult ADHD (n = 53), only childhood ADHD (n = 56) and healthy controls (n = 320). The Korean Adult ADHD Scale, Korean Wender-Utah Rating Scale, Beck Depression Inventory-II, Beck Anxiety Inventory, Barratt Impulsiveness Scale, Korean Young Internet Addiction Scale, and Temperament Character Inventory-Revised (TCI-R; based on Cloninger's seven factor model of temperament and character) were used to evaluate psychopathological factors.
RESULTS: Participants with persistent adult ADHD symptoms had significantly higher levels of childhood ADHD, depression, anxiety and the Internet addiction symptoms than did the only-childhood ADHD and control groups. The adult ADHD group also had significantly higher tendencies toward novelty seeking, harm avoidance, and self-transcendence, as well as low self-directedness and cooperativeness.
CONCLUSIONS: Results suggest that persistent ADHD is associated with several unfavourable psychopathological, temperamental and characteristic factors. Therefore, thorough evaluation of these factors for childhood ADHD could help predict prognoses and provide treatment plans for preventing persistent ADHD into adulthood.

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Iran J Psychiatry. 2017;12:42-48.

EVALUATION OF KNOWLEDGE AND ATTITUDE OF PARENTS OF ATTENTION DEFICIT/HYPERACTIVITY DISORDER CHILDREN TOWARDS ATTENTION DEFICIT/HYPERACTIVITY DISORDER IN CLINICAL SAMPLES.

Dodangi N, Vameghi R, Habibi N.

Objective: Knowledge and attitude of parents about attention deficit/hyperactivity disorder (ADHD) is an important factor in management of the disorder in children. This study investigates the parents' knowledge and attitude towards ADHD, its symptoms, diagnosis, treatment and prognosis.
Method: In this cross-sectional descriptive study, the subjects were 150 parents (120 mother and 30 father) of ADHD children who were referred to a child psychiatry clinic affiliated in university of social welfare and

rehabilitation sciences in Tehran. The diagnosis was made by a child psychiatrist according to DSM-IV TR criteria. The parents completed a 40 items questionnaire that was prepared by the authors and assessed their knowledge and attitude towards ADHD and source of their information.
Results: The most common source of parent's information about ADHD was TV. The parent's knowledge about the symptoms of the disorder was relatively good. But in regard to diagnosis, treatment and prognosis of the disorder, they have very low knowledge and even incorrect beliefs. The parent's knowledge significantly correlated with their educational level (p=0.01).
Conclusion: In general, knowledge of the parents was low and it can lead to misdiagnosis or mismanagement of this common and important disorder and need to further consideration in terms of educating parents about the disorder in media specially TV

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Ir J Med Sci. 2017;186:S38-S39.

ADHD IN CAMHS IN IRELAND: AN EVALUATION OF CURRENT PRACTICE.

Ahmad Shafiai SA, Neto FH, Gavin B, et al.

ADHD accounts for up to 1/3rd of presentations to CAMHS [1]. Recommended treatment is multi-modal combining medication and parenting [2]. This study aimed to compare the most recently available published HSE data [1] with current ADHD case load and typical management of ADHD by HSE region. A study specific questionnaire was designed and sent to all Consultant Child Psychiatrists (N = 71). Data analysed included information on dedicated ADHD clinics, estimated ADHD open case, and typical treatments offered. 34 consultants responded (response rate 48%). 26 (76%) operated a dedicated ADHD clinic, with an average of 88 ADHD cases per respondent. 24 consultants (71%) reported 'usually or always' initiating medication and 16 (47%) parenting groups. Fewer 'usually or always' offered either occupational (10, 29%) or speech and language therapy (6, 18%). Comparing practice in 2016 with earlier records, suggest similar rates of dedicated clinics (80% in 2011; 78% in 2012), although significant regional variation existed. Open ADHD case load was 3025 in Nov. 2011 and 2710 in 2012, giving a rate of 54 cases in 2011 and 47 in 2012 per CAMHS team. There was no standardised treatment data collected in the HSE reports. This postal survey adds some additional data to the management of ADHD in CAMHS with regional variation, but is limited by the restricted focus, respondent report and moderate response rate. It highlights the importance of clinical audits and national systems collecting standardized data on clinical treatment and outcomes to ensure services are providing effective and evidenced based care

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Ir J Med Sci. 2017;186:S7.

EXPLORING THE INTERFACE OF CARE FOR CHILDREN WITH ATTENTION DEFICIT/ HYPERACTIVITY DISORDER (ADHD): AN INTEGRATIVE REVIEW.

Heffron V, Brenner M, Frazer K, et al.

The UN Convention on the Rights of the Child defines the highest attainable standard of health care as a fundamental right of every child. The extent to which this requirement is met in practice by national health care systems varies considerably among the countries of Europe, and is the core purpose of the Horizon 2020 funded project Models Of Child Health Appraised (MOCHA). One aspect of the MOCHA study is to examine the interface of care for children with ADHD. We have carried out an integrative review of peer-reviewed literature on the interface between primary and secondary care for children and adolescents with ADHD. This covers assessment, diagnosis, treatment, on-going management and follow up care. A total of 1042 non-duplicate citations were screened for their relevance to this study, of which 17 were included in the study. Key themes identified were: the requirement for increased education for all professionals involved; the primary care provider should be the key professional involved, with access to secondary care when required; a care coordinator should liaise between primary and secondary care on behalf of the patient and parents; and cases should be managed by a multi-disciplinary team. In conclusion, the assessment, diagnosis, treatment and on-going management of ADHD varies across countries in Europe and around the world. This project identifies some key themes emerging from the most recent peer-reviewed literature on the integrative

care pathways being used in ADHD. Action on these themes could institute a more efficient service for patients with ADHD

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J Abnorm Child Psychol. 2016 Nov;44:1559-71.

COMPETING FACTOR MODELS OF CHILD AND ADOLESCENT PSYCHOPATHOLOGY.

Doyle MM, Murphy J, Shevlin M.

Co-occurring psychological disorders are highly prevalent among children and adolescents. To date, the most widely utilised factor model used to explain this co-occurrence is the two factor model of internalising and externalising (Achenbach 1966). Several competing models of general psychopathology have since been reported as alternatives, including a recent three factor model of Distress, Fear and Externalising Dimensions (Krueger 1999). Evidence for the three factor model suggests there are advantages to utilising a more complex model. Using the British Child and Adolescent Mental Health Survey 2004 data (B-CAMHS; N = 7997), confirmatory factor analysis was used to test competing factor structure models of child and adolescent psychopathology. The B-CAMHS was an epidemiological survey of children between the ages of 5 and 16 in Great Britain. Child psychological disorders were assessed using the Strength and Difficulties Questionnaire (Goodman 1997), and the Development and Wellbeing Assessment (Goodman et al. 2000). A range of covariates and risk variables including trauma, parent mental health and family functioning where subsequently utilised within a MIMIC model framework to predict each dimension of the 2 and three factor structure models. Two models demonstrated acceptable fit. The first complimented Achenbach's Internalising and Externalising structure. The three factor model was found to have highly comparable fit indices to the two factor model. The second order models did not accurately represent the data nor did an alternative three factor model of Internalising, Externalising and ADHD. The two factor and three factor MIMIC models observed unique profiles of risk for each dimension. The findings suggest that child and adolescent psychopathology may also be accurately conceptualised in terms of distress, fear and externalising dimensions. The MIMIC models demonstrated that the Distress and Fear dimensions have their own unique etiological profile of risk. This study directly informs future measurement models of child and adolescent psychopathology and demonstrates the effectiveness of a three factor model

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J Abnorm Child Psychol. 2016 Jul;44:923-35.

IDENTIFYING UNIQUE VERSUS SHARED PRE- AND PERINATAL RISK FACTORS FOR ASD AND ADHD USING A SIMPLEX-MULTIPLEX STRATIFICATION.

Oerlemans AM, Burmanje MJ, Franke B, et al.

Autism spectrum disorder (ASD) and attention-deficit/hyperactivity disorder (ADHD) frequently co-occur. Besides shared genetic factors, pre- and perinatal risk factors (PPFs) may determine if ASD, ADHD, or the combination of both disorders becomes manifest. This study aimed to test shared and unique involvement of PPFs for ASD and ADHD, using an approach that stratifies the sample into affected/unaffected offspring and single-incidence (SPX) versus multi-incidence (MPX) families. Pre- perinatal data based on retrospective parent-report were collected in 288 children (71 % males) from 31 SPX and 59 MPX ASD families, 476 children (65 % males) from 31 SPX and 171 MPX ADHD families, and 408 control children (42 % males). Except for large family size and more firstborns amongst affected offspring, no shared PFFs were identified for ASD and ADHD. PPFs predominantly related to ASD (maternal infections and suboptimal condition at birth) were more often reported in affected than unaffected siblings. PPFs associated with ADHD (low parental age, maternal diseases, smoking and stress) were shared between affected and unaffected siblings. Firstborn-ship was more frequent in SPX than MPX ASD probands. Our results suggest that the co-morbidity of ASD and ADHD is not likely explained by shared PPFs. Instead, PPFs might play a crucial role in the developmental pathways leading up to either disorder. PPFs in ADHD appear to index an increased shared

risk, whereas in ASD PPFs possibly have a more determining role in the disorder. SPX-MPX stratification detected possible etiological differences in ASD families, but provided no deeper insight in the role of PPFs in ADHD

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J Abnorm Child Psychol. 2016 Oct;44:1375-86.

DISINHIBITED ATTACHMENT DISORDER IN UK ADOPTED CHILDREN DURING MIDDLE CHILDHOOD: PREVALENCE, VALIDITY AND POSSIBLE DEVELOPMENTAL ORIGIN.

Kay C, Green J, Sharma K.

We investigate the prevalence, specificity and possible aetiology of Disinhibited Attachment Disorder (DAD) in adopted children without a history of institutional care. Sixty children adopted from UK out-of-home care (AD; mean age 102 months, 45 % male); 26 clinic-referred children with externalizing disorder (ED; mean age 104 months, 77 % male) but no history of maltreatment or disrupted care; and 55 matched low-risk comparison controls (LR; mean age 108 months, 49 % male) were assessed for DAD using a triangulation of parent, teacher, and research observations. Maltreatment history and child psychiatric symptoms were obtained from parent report and child language development was assessed. DAD was identified in 49 % of AD, 4 % of ED and 6 % of LR children. Seventy-two percent of AD children had suffered maltreatment. DAD was not associated with degree of risk exposure, demographics, or language. A significant association with ADHD did not explain variance in DAD prevalence across groups. DAD was significantly more common in children first admitted to out-of-home care between 7 and 24 months, independent of maltreatment severity, age at adoption and number of care placements. Implications for developmental theory, adoption policy and clinical application are discussed

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J Abnorm Child Psychol. 2016 Aug;44:1185-96.

COGNITIVE CONTROL DEFICITS IN SHIFTING AND INHIBITION IN PRESCHOOL AGE CHILDREN ARE ASSOCIATED WITH INCREASED DEPRESSION AND ANXIETY OVER 7.5 YEARS OF DEVELOPMENT.

Kertz SJ, Belden AC, Tillman R, et al.

Although depression and anxiety are common in youth (Costello et al. 2003), factors that put children at risk for such symptoms are not well understood. The current study examined associations between early childhood cognitive control deficits and depression and anxiety over the course of development through school age. Participants were 188 children (at baseline M = 5.42 years, SD = 0.79 years) and their primary caregiver. Caregivers completed ratings of children's executive functioning at preschool age and measures of depression and anxiety severity over seven assessment waves (a period of approximately 7.5 years). Longitudinal multilevel linear models were used to examine the effect of attention shifting and inhibition deficits on depression and anxiety. Inhibition deficits at preschool were associated with significantly greater depression severity scores at each subsequent assessment wave (up until 7.5 years later). Inhibition deficits were associated with greater anxiety severity from 3.5 to 7.5 years later. Greater shifting deficits at preschool age were associated with greater depression severity up to 5.5 years later. Shifting deficits were also associated with significantly greater anxiety severity up to 3.5 years later. Importantly, these effects were significant even after accounting for the influence of other key predictors including assessment wave/time, gender, parental education, IQ, and symptom severity at preschool age, suggesting that effects are robust. Overall, findings indicate that cognitive control deficits are an early vulnerability factor for developing affective symptoms. Timely assessment and intervention may be beneficial as an early prevention strategy

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J Abnorm Child Psychol. 2016 Oct;44:1425-38.

ACADEMIC AND SOCIAL FUNCTIONING ASSOCIATED WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER: LATENT CLASS ANALYSES OF TRAJECTORIES FROM KINDERGARTEN TO FIFTH GRADE.

Dupaul GJ, Morgan PL, Farkas G, et al.

Children with attention-deficit/hyperactivity disorder (ADHD) are known to exhibit significantly lower academic and social functioning than other children. Yet the field currently lacks knowledge about specific impairment trajectories experienced by children with ADHD, which may constrain early screening and intervention effectiveness. Data were analyzed from a nationally representative U.S. cohort in the Early Childhood Longitudinal Study, Kindergarten Class of 1998-1999 (ECLS-K) for 590 children (72.7 % male) whose parents reported a formal diagnosis of ADHD. Children's math, reading, and interpersonal skills were assessed at 5 time points between kindergarten and fifth grade. Growth mixture model analyses indicated 4 latent trajectory classes for reading, 8 classes for math, and 4 classes for interpersonal skills. Membership in reading and math trajectory classes was strongly related; overlaps with interpersonal skills classes were weaker. Trajectory class membership was correlated with demographic characteristics and behavioral functioning. Children with ADHD display substantial heterogeneity in their reading, math, and interpersonal growth trajectories, with some groups of children especially likely to display relatively severe levels of academic and social impairment over time. Early screening and intervention to address impairment, particularly reading difficulties, among kindergarten students with ADHD is warranted

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J Appl Behav Anal. 2016 Sep;49:596-616.

COMPARISONS OF SYNTHESIZED AND INDIVIDUAL REINFORCEMENT CONTINGENCIES DURING FUNCTIONAL ANALYSIS.

Fisher WW, Greer BD, Romani PW, et al.

Researchers typically modify individual functional analysis (FA) conditions after results are inconclusive (Hanley, Iwata, & McCord, 2003). Hanley, Jin, Vanselow, and Hanratty (2014) introduced a marked departure from this practice, using an interview-informed synthesized contingency analysis (IISCA). In the test condition, they delivered multiple contingencies simultaneously (e.g., attention and escape) after each occurrence of problem behavior; in the control condition, they delivered those same reinforcers noncontingently and continuously. In the current investigation, we compared the results of the IISCA with a more traditional FA in which we evaluated each putative reinforcer individually. Four of 5 participants displayed destructive behavior that was sensitive to the individual contingencies evaluated in the traditional FA. By contrast, none of the participants showed a response pattern consistent with the assumption of the IISCA. We discuss the implications of these findings on the development of accurate and efficient functional analyses

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J Child Sex Abus. 2016 Apr;25:276-92.

DOES INFORMATION ABOUT NEUROPSYCHIATRIC DIAGNOSES INFLUENCE EVALUATION OF CHILD SEXUAL ABUSE ALLEGATIONS?

Lainpelto K, Isaksson J, Lindblad F.

This study aimed at investigating if attitudes toward children with neuropsychiatric disorders influence evaluations concerning allegations of child sexual abuse. Law students (n = 107) at Stockholm University, Sweden, were presented a transcript of a mock police interview with a girl, 11 years of age. This interview was based on a real case, selected as a "typical" example from these years concerning contributions from the interviewer and the alleged victim. After having read the transcript, the students responded to a questionnaire concerning degree of credibility, if the girl talked about events that had really occurred, richness of details, and if the narrations were considered truthful and age-adequate. Fifty-four of the students were also told that the girl had been given the diagnoses of attention deficit/hyperactivity disorder and Asperger syndrome. Students who were informed about the diagnoses gave significantly lower scores concerning credibility of the interviewee. To a lesser degree they regarded her narrations as expressions of what had really occurred and considered her statements less truthful. Furthermore, they found that the narrations

contained fewer details. Finally, they found the girl less competent to tell about abuse. We conclude that a neuropsychiatric disorder may infer risks of unjustified skeptical attitudes concerning trustworthiness and cognitive capacity

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J Epidemiol. 2017 Feb;27:56-62.

CHANGE IN HOUSEHOLD INCOME AND RISK FOR ATTENTION DEFICIT HYPERACTIVITY DISORDER DURING CHILDHOOD: A NATIONWIDE POPULATION-BASED COHORT STUDY.

Choi Y, Shin J, Cho KH, et al.

BACKGROUND: Childhood attention deficit hyperactivity disorder (ADHD) is reported to be more prevalent among socioeconomically disadvantaged groups in various countries. The effect of poverty on child development appears to depend on how long poverty lasts. The timing of poverty also seems to be important for childhood outcomes. Lifetime socioeconomic status may shape current health. Thus, we investigated the effects of household income changes from birth to 4 years on the occurrence of ADHD.

METHODS: Data were obtained from 18,029 participants in the Korean National Health Insurance cohort who were born in 2002 and 2003. All individuals were followed until December 2013 or the occurrence of ADHD, whichever came first. Household income trajectories were estimated using the national health insurance premium and the group-based model. Cox proportional hazard models were used to compare incidence rates between different income trajectory groups after adjustment for possible confounding risk factors.

RESULTS: Of 18,029 participants, 554 subjects (3.1%) were identified as having ADHD by age 10 or 11. Seven household income trajectories within three categories were found. Children living in decreasing, consistently low, and consistently mid-low income households had an increased risk of ADHD compared to children who consistently lived in the mid-high household income group.

CONCLUSIONS: Children who live in decreasing-income or consistently low-income households have a higher risk for ADHD. Promotion of targeted policies and priority support may help reduce ADHD in this vulnerable group

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J Gambl Stud. 2016 Jun;32:591-604.

THE RELATIONSHIP BETWEEN PROBLEM GAMBLING AND ATTENTION DEFICIT HYPERACTIVITY DISORDER.

Waluk OR, Youssef GJ, Dowling NA.

Recent studies indicate that treatment-seeking problem gamblers display elevated rates of ADHD and that adolescents who screen positive for ADHD are more likely to engage in gambling, develop gambling problems, and experience a greater severity in gambling problems. This study aimed to (a) compare the prevalence of ADHD in treatment-seeking problem gamblers to the general population; (b) investigate the relationships between ADHD and problem gambling severity, cluster B personality disorders, motor impulsivity, alcohol use, substance use, gender, and age; and (c) investigate the degree to which these factors moderate the relationship between ADHD and problem gambling severity. Participants included 214 adults (154 males, 58 females, 2 unspecified) who sought treatment for their gambling problems at a specialist gambling agency in Melbourne, Australia. Almost one-quarter (24.9 %) of treatment-seeking problem gamblers screened positively for ADHD, which was significantly higher than the 14 % prevalence in a community sample. ADHD was significantly positively correlated with problem gambling severity, motor impulsivity, and cluster B personality disorders, but was not associated with alcohol and substance use, gender or age. None of the factors significantly moderated the relationship between ADHD and problem gambling severity. These findings suggest that a considerable proportion of treatment-seeking problem gamblers report ADHD and that their clinical profile is complicated by the presence of high impulsivity and

cluster B personality disorders. They highlight the need for specialist gambling agencies to develop screening, assessment, and management protocols for co-occurring ADHD to enhance the effectiveness of treatment

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J Korean Med Sci. 2017 Mar;32:401-06.

PREVALENCE OF ATTENTION-DEFICIT/HYPERACTIVITY DISORDER AND ITS COMORBIDITY AMONG KOREAN CHILDREN IN A COMMUNITY POPULATION.

Kim MJ, Park I, Lim MH, et al.

The aim of this study was to determine the prevalence of attention deficit hyperactivity disorders (ADHD) in children according to socio-demographic factors and the distribution of ADHD subtypes in a community in Korea. A screening survey using the Korean version of ADHD Rating Scale (K-ARS) was conducted between 2007 and 2008, and clinical interviews by a pediatric psychiatrist were performed for selected children between 2009 and 2010. A total of 49,573 elementary school students, between ages of 7 and 12, constituted the target population, among which 38,365 students (77.2%) and respective parents gave consent to participate. Of the participants, 200 screened children were clinically examined to confirm the diagnosis of ADHD. We estimated the prevalence of ADHD and its comorbidity in the population, after adjusting for nonresponse and nonparticipation. The prevalence of ADHD was 11.7% in boys and 5.2% in girls, with an overall prevalence of 8.5%. The combined type of inattentive and hyperactive was the most frequent at 4.7% of the whole population. Children were more likely to have ADHD if their parents were separated and had less education. Most commonly combined comorbidity was autism spectrum disorder (ASD) (10.1%). The prevalence of ADHD in the school-aged population is an essential information for improving the quality of public health mental services for evaluation and treatment of ADHD

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J Korean Med Sci. 2017 Mar;32:514-21.

COMPARISON OF QEEG FINDINGS BETWEEN ADOLESCENTS WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER (ADHD) WITHOUT COMORBIDITY AND ADHD COMORBID WITH INTERNET GAMING DISORDER.

Park JH, Hong JS, Han DH, et al.

Internet gaming disorder (IGD) is often comorbid with attention deficit hyperactivity disorder (ADHD). In this study, we compared the neurobiological differences between ADHD comorbid with IGD (ADHD+IGD group) and ADHD without comorbidity (ADHD-only group) by analyzing quantitative electroencephalogram (QEEG) findings. We recruited 16 male ADHD+IGD, 15 male ADHD-only adolescent patients, and 15 male healthy controls (HC group). Participants were assessed using Young's Internet Addiction Scale and ADHD Rating Scale. Relative power and inter- and intra-hemispheric coherences of brain waves were measured using a digital electroencephalography (EEG) system. Compared to the ADHD-only group, the ADHD+IGD group showed lower relative delta power and greater relative beta power in temporal regions. The relative theta power in frontal regions were higher in ADHD-only group compared to HC group. Inter-hemispheric coherence values for the theta band between F3-F4 and C3-C4 electrodes were higher in ADHD-only group compared to HC group. Intra-hemispheric coherence values for the delta, theta, alpha, and beta bands between P4-O2 electrodes and intra-hemispheric coherence values for the theta band between Fz-Cz and T4-T6 electrodes were higher in ADHD+IGD group compared to ADHD-only group. Adolescents who show greater vulnerability to ADHD seem to continuously play Internet games to unconsciously enhance attentional ability. In turn, relative beta power in attention deficit in ADHD+IGD group may become similar to that in HC group. Repetitive activation of brain reward and working memory systems during continuous gaming may result in an increase in neuronal connectivity within the parieto-occipital and temporal regions for the ADHD+IGD group

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J Med Life. 2016 Oct;9:373-79.

EFFECTS OF A SELECTED EXERCISE PROGRAMON EXECUTIVE FUNCTION OF CHILDREN WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER.

Memarmoghaddam M, Torbati HT, Sohrabi M, et al.

Introduction. The aim of this study was to examine the effectiveness of a Selected exercise program on the executive function of children with ADHD.

Method. The participants were 40 male students, aged 7-11 years. The participants were randomly assigned into two groups (experimental and control). The experimental group participated in an exercise program for 24 sessions, 90 minutes per session. The control group did not receive any intervention. Before and after the exercise period, all the participants were assessed with Stroop and Go-No-Go tests, and the resulting data were analyzed by using MANCOVA.

Result. The results showed that the cognitive inhibition of the children in the experimental group was significantly different compared with the control group ($p < 0.05$). Additionally, there was a significant difference between the experimental and control groups in the behavioral inhibition ($p < 0.05$).

Conclusion. An organized physical activity helps to improve the executive function in children with ADHD

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J Neurosurg Pediatr. 2017 Jan;19:38-45.

CLINICAL PREDICTORS OF VESTIBULO-OCULAR DYSFUNCTION IN PEDIATRIC SPORTS-RELATED CONCUSSION.

Ellis MJ, Cordingley DM, Vis S, et al.

OBJECTIVE There were 2 objectives of this study. The first objective was to identify clinical variables associated with vestibulo-ocular dysfunction (VOD) detected at initial consultation among pediatric patients with acute sports-related concussion (SRC) and postconcussion syndrome (PCS). The second objective was to reexamine the prevalence of VOD in this clinical cohort and evaluate the effect of VOD on length of recovery and the development of PCS.

METHODS A retrospective review was conducted for all patients with acute SRC and PCS who were evaluated at a pediatric multidisciplinary concussion program from September 2013 to May 2015. Acute SRS was defined as presenting < 30 days postinjury, and PCS was defined according to the International Classification of Diseases, 10th Revision criteria and included being symptomatic 30 days or longer postinjury. The initial assessment included clinical history and physical examination performed by 1 neurosurgeon. Patients were assessed for VOD, defined as the presence of more than 1 subjective vestibular and oculomotor complaint (dizziness, diplopia, blurred vision, etc.) and more than 1 objective physical examination finding (abnormal near point of convergence, smooth pursuits, saccades, or vestibulo-ocular reflex testing). Poisson regression analysis was used to identify factors that increased the risk of VOD at initial presentation and the development of PCS.

RESULTS Three hundred ninety-nine children, including 306 patients with acute SRC and 93 with PCS, were included. Of these patients, 30.1% of those with acute SRC (65.0% male, mean age 13.9 years) and 43.0% of those with PCS (41.9% male, mean age 15.4 years) met the criteria for VOD at initial consultation. Independent predictors of VOD at initial consultation included female sex, preinjury history of depression, posttraumatic amnesia, and presence of dizziness, blurred vision, or difficulty focusing at the time of injury. Independent predictors of PCS among patients with acute SRC included the presence of VOD at initial consultation, preinjury history of depression, and posttraumatic amnesia at the time of injury.

CONCLUSIONS This study identified important potential risk factors for the development of VOD following pediatric SRC. These results provide confirmatory evidence that VOD at initial consultation is associated with prolonged recovery and is an independent predictor for the development of PCS. Future studies examining clinical prediction rules in pediatric concussion should include VOD. Additional research is needed to elucidate the natural history of VOD following SRC and establish evidence-based indications for targeted vestibular rehabilitation

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Journal of Advanced Pharmaceutical Technology and Research. 2016;7:144-48.

COMPARISON OF THE EFFECTS OF METHYLPHENIDATE AND THE COMBINATION OF METHYLPHENIDATE AND RISPERIDONE IN PRESCHOOL CHILDREN WITH ATTENTION-DEFICIT HYPERACTIVITY DISORDER.

Safavi P, Dehkordi AH, Ghasemi N.

Attention-deficit hyperactivity disorder (ADHD) is a common psychiatric disorder among preschool children but the number of controlled clinical trials regarding psychopharmacological treatment in this age group is limited. The aim of this study was to compare methylphenidate with the combination of methylphenidate and risperidone in preschool children with ADHD. Forty-two preschool children, aged 3-6 years, diagnosed with ADHD by a child and adolescent psychiatrist according to the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition-Text Revision criteria, were enrolled in a 6-week, single-blind clinical trial and administered with methylphenidate (5-30 mg/dl) or the combination of methylphenidate and risperidone (0.25-2 mg/dl) in Iran. Treatment outcomes were assessed using the Conners' Rating Scale and Clinical Global Impression (CGI) Scale at baseline and 3 and 6 weeks after starting the drugs administration. Side effects were rated by a checklist and body weight was measured at each visit. There were no significant differences between the two protocols in Parent Conners' Rating Scale scores ($P > 0.05$) and CGI scores ($P > 0.05$). Both groups showed a significant improvement in ADHD symptoms over the 6 weeks of treatment for Parent Conners' Rating Scale ($P < 0.001$). The combination group used significantly lower doses of methylphenidate compared to the other group ($P = 0.002$). The most common adverse effects were anorexia (21.7%) and daytime drowsiness (17.4%) in combination treatment group and insomnia (33.3%) and anorexia (25%) in methylphenidate group. Risperidone and methylphenidate may be effective and well tolerated in preschool children with ADHD, and adding risperidone to methylphenidate may decrease the occurrence of some side effects of methylphenidate such as insomnia and anorexia and lower the dose of methylphenidate may be needed to control symptoms

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J Affective Disord. 2017;215:281-87.

IRRITABILITY IN ADHD: ASSOCIATIONS WITH DEPRESSION LIABILITY.

Eyre O, Langley K, Stringaris A, et al.

Background Irritability and the new DSM-5 diagnostic category of Disruptive Mood Dysregulation Disorder (DMDD) have been conceptualised as related to mood disorder. Irritability is common in Attention Deficit Hyperactivity Disorder (ADHD) but little is known about its association with depression risk in this group. This study aims to establish levels of irritability and prevalence of DMDD in a clinical sample of children with ADHD, and examine their association with anxiety, depression and family history of depression.

Methods The sample consisted of 696 children (mean age 10.9 years) with a diagnosis of ADHD, recruited from UK child psychiatry and paediatric clinics. Parents completed the Child and Adolescent Psychiatric Assessment, a semi-structured diagnostic interview, about their child. This was used to establish prevalence of DMDD, anxiety disorder and depressive disorder, as well as obtain symptom scores for irritability, anxiety and depression. Questionnaires assessed current parental depression, and family history of depression.

Result Irritability was common, with 91% endorsing at least one irritable symptom. 3-month DMDD prevalence was 31%. Children with higher levels of irritability or DMDD were more likely to have comorbid symptoms of anxiety, depression and a family history of depression. Limitations Results are based on a clinical sample, so may not be generalizable to children with ADHD in the general population.

Conclusions Irritability and DMDD were common, and were associated with markers of depression liability. Longitudinal studies are needed to examine the association between irritability and depression in youth with ADHD as they get older

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J Affective Disord. 2017;215:230-36.

NICE GUYS: HOMOZYGOCITY FOR THE TPH2 -703G/T (RS4570625) MINOR ALLELE PROMOTES LOW AGGRESSIVENESS AND LOW ANXIETY.

Laas K, et al.

Background Tryptophan hydroxylase (TPH) is the rate-limiting enzyme in the synthesis of serotonin. We examined whether the TPH2 polymorphism -703G/T (rs4570625) is associated with aggressiveness and impulsivity, and the prevalence of psychiatric disorders, in a population-representative sample.

Methods We used self and proxy reports on aggressive behaviour in the younger birth cohort of the longitudinal Estonian Children Personality, Behaviour and Health Study collected at age 25, and earlier collected impulsivity and related data of both ECPBHS cohorts.

Results The TT homozygous males reported less aggressive behaviour in the Life History of Aggression interview at age 25. They also had significantly lower scores in Illinois Bully Scale peer reports, and less ADHD symptoms rated by teachers both at ages 9 and 15. The TT homozygotes of both sexes had the lowest Maladaptive Impulsivity at ages 18 and 25, and the highest Adaptive Impulsivity at age 25. The TT homozygotes also had low depressiveness and trait anxiety by age 25, and the odds ratio for the prevalence of anxiety disorders was 9.38 for the G-allele carriers. Limitations The main limitation of the study is the naturally occurring low number of subjects with the TT genotype.

Conclusions Subjects with the TPH2 rs4570625 TT genotype, especially males, exhibit less aggression and a favourable impulsivity profile, and develop anxiety disorders by young adulthood less often

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J Autism Dev Disord. 2017;1-14.

ATYPICAL PROCESSING OF GAZE CUES AND FACES EXPLAINS COMORBIDITY BETWEEN AUTISM SPECTRUM DISORDER (ASD) AND ATTENTION DEFICIT/HYPERACTIVITY DISORDER (ADHD).

Groom MJ, Kochhar P, Hamilton A, et al.

This study investigated the neurobiological basis of comorbidity between autism spectrum disorder (ASD) and attention deficit/hyperactivity disorder (ADHD). We compared children with ASD, ADHD or ADHD+ASD and typically developing controls (CTRL) on behavioural and electrophysiological correlates of gaze cue and face processing. We measured effects of ASD, ADHD and their interaction on the EDAN, an ERP marker of orienting visual attention towards a spatially cued location and the N170, a right-hemisphere lateralised ERP linked to face processing. We identified atypical gaze cue and face processing in children with ASD and ADHD+ASD compared with the ADHD and CTRL groups. The findings indicate a neurobiological basis for the presence of comorbid ASD symptoms in ADHD. Further research using larger samples is needed

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J Child Fam Stud. 2017 Mar;26:950-60.

CHARACTERISTICS OF PARENTS OF CHILDREN WITH ADHD WHO NEVER ATTEND, DROP OUT, AND COMPLETE BEHAVIORAL PARENT TRAINING.

Chacko A, Wymbs BT, Rajwan E, et al.

Behavioral parent training (BPT) is an evidence-based intervention for the treatment of attention-deficit/hyperactivity disorder and related disruptive behavior disorders in youth. Although efficacious, dropout from BPT is a notable issue, particular for high-risk families. The literature suggests that parental factors (stress, psychopathology and cognitions) may be particularly important in understanding which parents dropout from BPT. To date, however, limited attention has been given to how these factors may be related to dropout at varying points during BPT. Secondary data analyses from a completed clinical trial of a traditional BPT intervention is presented herein. Forty participants were classified into three groups based on timing of dropout from BPT (enrolled in but never attended BPT; dropped out during BPT, and completed BPT). Parent-level factors (stress, depressive symptoms, parental efficacy, and parental attributions for child behavior) were assessed at baseline and post-treatment (parental perceived barriers to treatment) to determine if these factors were differentially related to dropout group status. Results suggested that parents who never attended BPT were more likely to have lower parental efficacy and greater maladaptive

attributions regarding their child compared to parents who dropped out from BPT and those who completed BPT. Moreover, parents perceptions of the relevance of BPT was lower in the never attended group and the dropped out from BPT group compared to the completed BPT group. Results of the study have implications for tailoring engagement strategies focused on parental cognitions throughout the process of BPT, particularly for high-risk families

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J Child Psychol Psychiatry. 2017 Mar;58:240-47.

MATERNAL PREPREGNANCY BODY MASS INDEX AND OFFSPRING ATTENTION-DEFICIT/HYPERACTIVITY DISORDER: A QUASI-XPERIMENTAL SIBLING-COMPARISON, POPULATION-BASED DESIGN.

Musser ED, Willoughby MT, Wright S, et al.

BACKGROUND: High maternal prepregnancy body mass index (BMI) has been associated with increased risk of offspring attention-deficit/hyperactivity disorder (ADHD). However, whether this effect is attributable to maternal or familial level confounds has been little examined.

METHODS: The present study sought to examine these associations, utilizing data from the medical records of a health care system which treats 350,000 patients annually and a sibling-comparison design in a sample of 4,682 children born to 3,645 mothers.

RESULTS: When examining the overall maternal effect, a linear association was observed between maternal prepregnancy BMI and child ADHD [b = 0.04, 95% confidence interval (95% CI) = 0.02-0.06, p = .0003], such that a one-unit (i.e. 1 kg/m2) increase in prepregnancy BMI was associated with a 4% increase in the odds of ADHD (exp b = 1.04). However, when the model was reparameterized to take full advantage of the sibling design to allow for the examination of both maternal and child-specific effects, the child-specific prepregnancy BMI effect was not reliably different from zero (b = -0.08, 95% CI = -0.23 to 0.06, p = .24). In contrast, at the maternal-level, average prepregnancy BMI was a reliably non-zero predictor of child ADHD (b = 0.04, 95% CI = 0.02-0.06, p < .0001) with each one-unit increase in maternal prepregnancy BMI associated with a 4.2% increase in the odds of ADHD (exp b = 1.04, 95% CI = 1.02-1.06).

CONCLUSIONS: The association between maternal prepregnancy BMI and offspring ADHD may be better accounted for by familial or maternal confounds rather than a direct causal effect of BMI.

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J Child Psychol Psychiatry. 2017 Mar;58:248-57.

EVIDENCE FOR INCREASED BEHAVIORAL CONTROL BY PUNISHMENT IN CHILDREN WITH ATTENTIONÂ€• DEFICIT HYPERACTIVITY DISORDER.

Furukawa E, Alsop B, Sowerby P, et al.

Background: The behavioral sensitivity of children with ADHD to punishment has received limited theoretical and experimental attention. This study evaluated the effects of punishment on the response allocation of children with ADHD and typically developing children.

Method: Two hundred and ten children, 145 diagnosed with ADHD, completed an operant task in which they chose between playing two simultaneously available games. Reward was arranged symmetrically across the games under concurrent variable interval schedules. Asymmetric punishment schedules were superimposed; responses on one game were punished four times as often as responses on the other.

Results: Both groups allocated more of their responses to the less frequently punished alternative. Response bias increased significantly in the ADHD group during later trials, resulting in missed reward trials and reduced earnings.

Conclusions: Punishment exerted greater control over the response allocation of children with ADHD with increased time on task. Children with ADHD appear more sensitive to the cumulative effects of punishment than typically developing children

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J Child Psychol Psychiatry. 2017 Mar;58:231-39.

FAMILIAL AGGREGATION OF ATTENTIONÂ€• DEFICIT/HYPERACTIVITY DISORDER.

Chen Q, Brikell I, Lichtenstein P, et al.

Background: Attention-deficit/hyperactivity disorder (ADHD) aggregates in families. To date, the strength, pattern, and characteristics of the familial aggregation have not been thoroughly assessed in a population-based family sample.

Methods: In this cohort study, we identified relative pairs of twins, full and half-siblings, and full and half cousins from 1,656,943 unique individuals born in Sweden between 1985 and 2006. The relatives of index persons were followed from their third birthday to 31 December 2009 for ADHD diagnosis. Birth year adjusted hazard ratio (HR), that is, the rate of ADHD in relatives of ADHD-affected index persons compared with the rate of ADHD in relatives of unaffected index persons, was estimated in the different types of relatives using Cox proportional hazards model.

Results: During the follow-up, 31,865 individuals were diagnosed with ADHD (male to female ratio was 3.7). The birth year adjusted HRs were as follows: 70.45 for monozygotic twins; 8.44 for dizygotic twins; 8.27 for full siblings; 2.86 for maternal half-siblings; 2.31 for paternal half-siblings; 2.24 for full cousins; 1.47 for half cousins. Maternal half-siblings had significantly higher HR than in paternal half-siblings. The HR did not seem to be affected by index person's sex. Full siblings of index persons with ADHD diagnosis present at age 18 or older had a higher rate of ADHD (HR: 11.49) than full siblings of index persons with ADHD diagnosis only before age 18 (HR: 4.68).

Conclusions: Familial aggregation of ADHD increases with increasing genetic relatedness. The familial aggregation is driven by not only genetic factors but also a small amount of shared environmental factors. Persistence of ADHD into adulthood indexes stronger familial aggregation of ADHD

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J Clin Exp Neuropsychol. 2017 Mar;39:296-312.

NEUROCOGNITIVE FUNCTIONING IN CHILDREN WITH DEVELOPMENTAL DYSLEXIA AND ATTENTION-DEFICIT/HYPERACTIVITY DISORDER: MULTIPLE DEFICITS AND DIAGNOSTIC ACCURACY.

Moura Ov, Pereira M, Alfaiate Cu, et al.

Introduction: This study aimed to investigate the neurocognitive functioning of children with developmental dyslexia (DD) and attention-deficit/hyperactivity disorder (ADHD).

Method: Four groups of children between the ages of 8 and 10 years participated in the study: typically developing children (TDC; N = 34), children with DD-only (N = 32), children with ADHD-only (N = 32), and children with DD + ADHD (N = 18).

Results: Children with DD and ADHD exhibited significant weaknesses on almost all neurocognitive measures compared with TDC. Large effect sizes were observed for naming speed and phonological awareness. The comorbid group showed deficits consistent with both DD and ADHD without additional impairments. Results from binary logistic regression and receiver-operating characteristic (ROC) curve analyses suggested that some neurocognitive measures revealed an adequate sensitivity for the clinical diagnosis of both neurodevelopmental disorders. Specifically, naming speed and phonological awareness were the strongest predictors to correctly discriminate both disorders.

Conclusions: Taken together, the results lend support to the multiple cognitive deficit hypothesis showing a considerable overlap of neurocognitive deficits between both disorders

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J Clin Child Adolesc Psychol. 2017 Mar;46:188-97.

STAGE 2 SLEEP EEG SIGMA ACTIVITY AND MOTOR LEARNING IN CHILDHOOD ADHD: A PILOT STUDY.

Saletin JM, Coon WG, Carskadon MA.

Attention deficit hyperactivity disorder (ADHD) is associated with deficits in motor learning and sleep. In healthy adults, overnight improvements in motor skills are associated with sleep spindle activity in the sleep electroencephalogram (EEG). This association is poorly characterized in children, particularly in pediatric ADHD. Polysomnographic sleep was monitored in 7 children with ADHD and 14 typically developing controls.

All children were trained on a validated motor sequence task (MST) in the evening with retesting the following morning. Analyses focused on MST precision (speedâ€“accuracy trade-off). NREM Stage 2 sleep EEG power spectral analyses focused on spindle-frequency EEG activity in the sigma (12â€“15 Hz) band. The ADHD group demonstrated a selective decrease in power within the sigma band. Evening MST precision was lower in ADHD, yet no difference in performance was observed following sleep. Moreover, ADHD status moderated the association between slow sleep spindle activity (12â€“13.5 Hz) and overnight improvement; spindle-frequency EEG activity was positively associated with performance improvements in children with ADHD but not in controls. These data highlight the importance of sleep in supporting next-day behavior in ADHD while indicating that differences in sleep neurophysiology may contribute to deficits in this population

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J Clin Child Adolesc Psychol. 2017 Mar;46:284-94.

ADHD AND SLEEP QUALITY: LONGITUDINAL ANALYSES FROM CHILDHOOD TO EARLY ADULTHOOD IN A TWIN COHORT.

Gregory AM, Agnew-Blais JC, Matthews T, et al.

Attention-deficit/hyperactivity disorder (ADHD) is associated with poor sleep quality, but there is more to learn about the longitudinal association and aetiology of this association. We investigated the following: (a) Is there an association between childhood ADHD and poor sleep quality in young adulthood? (b) Is this driven by the long-term effects of childhood ADHD or concurrent associations with ADHD in young adulthood? (c) To what extent do genetic and environmental influences explain the overlap between symptoms of ADHD and poor sleep quality? Participants were from the Environmental Risk Longitudinal Twin Study of 2,232 twin children born in the United Kingdom in 1994-1995. We ascertained ADHD diagnoses at ages 5, 7, 10, 12, and 18. We assessed sleep quality using the Pittsburgh Sleep Quality Index at age 18. We used regression models to examine longitudinal associations and bivariate twin modelling to test genetic and environmental influences. Children with ADHD had poorer sleep quality in young adulthood, but only if their ADHD persisted. Adults with ADHD had more sleep problems than those without ADHD, over and above psychiatric comorbidity and maternal insomnia. ADHD and sleep problems in young adulthood were associated because of genetic (55%) and nonshared environmental influences (45%). Should ADHD remit, children with ADHD do not appear to have an increased risk of later sleep problems. Good quality sleep is important for multiple areas of functioning, and a better understanding of why adults with ADHD have poorer sleep quality will further the goal of improving treatments

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J Clin Psychopharmacol. 2017;37:220-25.

EFFECT OF METHYLPHENIDATE ON EMOTIONAL DYSREGULATION IN CHILDREN WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER + OPPOSITIONAL DEFIANT DISORDER/CONDUCT DISORDER.

Kutlu A, Akyol Ardic U, Ercan ES.

Background and Aim Emotional dysregulation (ED) is a frequent feature of attention-deficit/hyperactivity disorder (ADHD). It can be observed as a dysregulation profile or a deficient emotional self-regulation (DESR) profile. Oppositional defiant disorder/conduct disorder (ODD/CD) comorbidity is prevalent in ADHD and known to be related with ED. The first-line treatment of ADHD includes psychostimulants, but their effects on ED are not well studied. This study aimed to evaluate the outcomes of methylphenidate (MPH) treatment on ED in ADHD + ODD/CD cases.

Methods A total of 118 ADHD + ODD/CD patients with a mean age of 9.0 ± 1.9 years were treated with MPH for 1 year. Also, parents of cases were recruited for a parent-training program, which initiated after first month of MPH treatment. Symptom severity was assessed at baseline and 12th month by Turgay Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition-Based Child and Adolescent Behavior Disorders Screening and Rating Scale-Parent Form, Children Depression Inventory, Child Behavior Checklist 4-18 years, and Parental Acceptance and Rejection Questionnaire-Mother Form.

Results Emotional dysregulation (DESR + DP) was present in 85.6% of cases. Conduct disorder was significantly higher in patients with DP, whereas ODD was significantly higher in the DESR and non-ED groups ($P < 0.0001$). Symptoms of ADHD and ED were significantly improved with 1-year of MPH treatment

(P < 0.05). The improvement in ED was independent of improvement in ADHD symptoms and parent training (P < 0.05).
Conclusions Emotional dysregulation is highly prevalent in disruptive behavioral disorders as ODD and CD, which are comorbid with ADHD. The MPH treatment is effective on ED independently from other clinical determinants

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J Clin Sleep Med. 2017;13:511-12.

CYCLIC ALTERNATING PATTERN ASSOCIATED WITH CATATHRENIA AND BRUXISM IN A 10-YEAR-OLD PATIENT.

Villafuerte-Trisolini B, et al.

Cyclic alternating pattern (CAP) is widely recognized as an expression of sleep instability in electroencephalogram activity during non-rapid eye movement sleep. We report a case with sequences of CAP followed by bruxism and catathrenia in a 10-y-old male patient with a diagnosis of attention deficit hyperactivity disorder in treatment with methylphenidate. We found CAP in 83.1% of all episodes of catathrenia, and the CAP rate was 12.8%. We propose to consider catathrenia as one of the sleep disorders that may be accompanied by CAP

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Journal of Electrocardiology. 2017.

THE EFFECT OF METILPHENIYDATE, RISPERIDONE AND COMBINATION THERAPY ON ECG IN CHILDREN WITH ATTENTION-DEFICIT HYPERACTIVITY DISORDER.

Karpuz D, Hallioglu O, Toros F, et al.

Introduction: This study is to investigate ventricular repolarization on electrocardiogram (ECG) in a pediatric population receiving methylphenidate (MPH), risperidone (RIS) and combined therapy.
Methods: A total of 215 patients between 6 and 12. years with ADHD/conduct disorder receiving methylphenidate, risperidone and combined therapy for minimum 3. months and an untreated ADHD group (n = 76) was consecutively included in the study. Twelve lead ECG parameters including mean QT, QTc, T-peak to T-end (TpTe) intervals, TpTe dispersion and TpTe/QT ratio were compared.
Results: QT interval, and QTc, TpTe interval, TpTe dispersion and TpTe/QTc ratio values for groups receiving RIS, MPH and combined therapy were found to be significantly higher than other groups. Moreover, in the combined therapy group TpTe and TpTe/QTc values were higher than the single drug administration groups (p. <. 0.05). TpTe and TpTe/QT ratio was significantly higher in the RIS group compared to that of the MPH group.
Conclusion: These results suggested that combined therapy of these drugs had a more prominent impact on the T wave and RIS could be strongly associated with it

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J Fam Psychother. 2017;1-12.

EFFECTIVENESS OF GROUP RESILIENCY TRAINING ON ANXIETY, DEPRESSION, AND MARITAL SATISFACTION IN MOTHERS OF CHILDREN WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER.

Kaveh Hojjat S, Monadi Ziarat H, Rezaei M, et al.

Many studies have been reported that higher levels of depression and anxiety in parents of children with attention deficit hyperactivity disorder. The objective of this study was to evaluate the effectiveness of group resiliency training on anxiety, depression, and marital satisfaction in mothers of children with attention deficit hyperactivity disorder. This study was an experimental, pretestΓÇöpost-test study with control group. Participants included 54 mothers of children with attention deficit hyperactivity disorder. Mothers were randomly divided to experimental and control groups. The experimental group received 8 group resiliency training sessions and then compared in changes in Beck depression and anxiety scale and the Enrich marital satisfaction scale. Results of multivariate analysis of covariance showed significant change in depression,

anxiety, and marital satisfaction. Our study indicates that resiliency training can be considered as one the effective intervention for anxiety, depression, and marital satisfaction in these mothers

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J Fam Psychother. 2017;1-17.

SLOVENIAN FAMILIES WITH CHILDREN WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER: INTERPERSONAL RELATIONS, PARENTS' ATTENTION-DEFICIT/HYPERACTIVITY DISORDER SYMPTOMS AND IMPLICATIONS FOR FAMILY THERAPY.

Bandel Castro T.

We aimed to assess interpersonal relationships within Slovenian families with a child diagnosed with attention-deficit/hyperactivity disorder (proband) as compared to control families. The current study evaluated parents' retrospective assessment of attention-deficit/hyperactivity disorder symptoms in childhood in both groups and possible predictive factors for the occurrence of attention-deficit/hyperactivity disorder in children. The proband parents experienced more difficulties in interpersonal relations, more often related to attention-deficit/hyperactivity disorder symptoms during their childhood and the proband children blamed themselves for marital conflict to a greater extent. The general functioning of families and parents' attention-deficit/hyperactivity disorder symptoms in their childhood are the most significant predictive factors for the occurrence of the disorder in children. These findings stressed the appropriateness of family therapy focused on interpersonal relationships in families with attention-deficit/hyperactivity disorder children

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Journal of Learning Disabilities. 2017 Mar;50:168-79.

RAPID NAMING AND PHONEMIC AWARENESS IN CHILDREN WITH OR WITHOUT READING DISABILITIES AND/OR ADHD.

De Groot BJA, Van den Bos KP, van der Meulen BF, et al.

Employing a large sample of children from Dutch regular elementary schools, this study assessed the contributing and discriminating values of reading disability (RD) and attention-deficit/hyperactivity disorder (ADHD) to two types of phonological processing skills, phonemic awareness (PA) and rapid automatized naming (RAN). A second objective was to investigate whether comorbidity of RD and ADHD should be considered as an additive phenomenon as to RAN and PA. A total of 1,262 children, aged 8 to 13 years, were classified as RD (n = 121), ADHD (n = 17), comorbid (RD+ADHD; n = 16), or control (n = 1,108). Phonological processing was assessed by standardized tests of PA and RAN. Disability groups were compared to each other and contrasted to the control group. Although results indicate substantial effects for all three disability groups on both types of phonological processing, and the RAN/PA compound measure in particular, effect sizes were considerably larger for the RD groups, as compared to the ADHD-only group. Theoretical and practical implications are discussed

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Journal of Pediatric Hematology/Oncology. 2017;39:e46-e53.

THE EFFECTS OF ATTENTION PROBLEMS ON PSYCHOSOCIAL FUNCTIONING IN CHILDHOOD BRAIN TUMOR SURVIVORS: A 2-YEAR POSTCRANIOSPINAL IRRADIATION FOLLOW-UP.

Oh Y, Seo H, Sung KW, et al.

Objective: To examine the psychosocial outcomes and impact of attention problems in survivors of pediatric brain tumor. Study Design: The survivors' cognitive functioning was measured using the Wechsler Intelligence Scale for Children. The Child Behavior Checklist-Attention Problems scale was used to screen for attention problems, and participants were classified as having attention problems (n=15) or normal attention (n=36). Psychosocial functioning was examined with the Korean Personality Rating scale for Children (K-PRC) at precraniospinal radiation and at 2-year follow-up. Results: The attention problem group showed significantly higher depression and externalizing symptoms (delinquency, hyperactivity) and more significant impairment in family relationships than did the normal attention group at baseline. At follow-up, the attention problem group demonstrated significantly more delinquency and impaired family and social

relationships. With the K-PRC scores, except for the somatization, social relationship subscale, there were significant differences between groups, but not in terms of treatment by time interaction or within time. At follow-up, multiple linear regressions showed that age at diagnosis significantly predicted K-PRC somatization (B=-1.7, P=0.004) and social relationships (B=-1.7, P=0.004), baseline full-scale intelligence quotient predicted K-PRC depression (B=-0.4, P=0.032) and somatization (B=-0.3, P=0.015), and attention problems at baseline predicted K-PRC depression (B=-15.2, P=0.036) and social relationships (B=-11.6, P=0.016). Conclusion: Pediatric brain tumor survivors, in particular, patients with attention problems, had worse psychosocial functioning at baseline and follow-up. Attention problems at baseline need to be carefully evaluated in assessing psychosocial functioning of pediatric brain tumor survivors

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J Pediatr. 2017.

CELIAC DISEASE IS ASSOCIATED WITH CHILDHOOD PSYCHIATRIC DISORDERS: A POPULATION-BASED STUDY.

Butwicka A, Lichtenstein P, Fris+®n L, et al.

Objectives: To determine the risk of future childhood psychiatric disorders in celiac disease, assess the association between previous psychiatric disorders and celiac disease in children, and investigate the risk of childhood psychiatric disorders in siblings of celiac disease probands.

Study design: This was a nationwide registry-based matched cohort study in Sweden with 10 903 children (aged <18 years) with celiac disease and 12 710 of their siblings. We assessed the risk of childhood psychiatric disorders (any psychiatric disorder, psychotic disorder, mood disorder, anxiety disorder, eating disorder, psychoactive substance misuse, behavioral disorder, attention-deficit hyperactivity disorder [ADHD], autism spectrum disorder [ASD], and intellectual disability). HRs of future psychiatric disorders in children with celiac disease and their siblings was estimated by Cox regression. The association between previous diagnosis of a psychiatric disorder and current celiac disease was assessed using logistic regression.

Results: Compared with the general population, children with celiac disease had a 1.4-fold greater risk of future psychiatric disorders. Childhood celiac disease was identified as a risk factor for mood disorders, anxiety disorders, eating disorders, behavioral disorders, ADHD, ASD, and intellectual disability. In addition, a previous diagnosis of a mood, eating, or behavioral disorder was more common before the diagnosis of celiac disease. In contrast, siblings of celiac disease probands were at no increased risk of any of the investigated psychiatric disorders.

Conclusions: Children with celiac disease are at increased risk for most psychiatric disorders, apparently owing to the biological and/or psychological effects of celiac disease

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J Pharm Pract. 2016;29:320.

PREVALENCE OF ATTENTION DEFICIT/HYPERACTIVITY DISORDER-LIKE PRESENTATION AMONG VETERANS.

Akulonis CM, Hieber R, Shuman M, et al.

Background: Attention deficit/ hyperactivity disorder (ADHD) is one of the most common psychological disorders presenting in children, but the study, diagnosis, and treatment of adult ADHD is rising. Two most recent estimates of the prevalence of ADHD in adults residing in the United States fall at 2.9 and 4.4%. Evidence suggests the prevalence of adult ADHD may be higher in the Veterans Affairs population. Adult ADHD may be more prevalent in undomiciled veterans and veterans with posttraumatic stress disorder, traumatic brain injury, substance use disorder, anxiety disorders, and depressive disorders. This pilot study will provide data for the Veterans Affairs population by surveying the prevalence of adult ADHD-like presentation in outpatient clinics, rather than in veterans with specific disease states.

Objectives: 1. Determine the prevalence of ADHD-like presentation in outpatient clinics of Captain James A. Lovell Federal Health Care Center (FHCC), 2. Identify correlates between ADHD symptoms and participants' demographic information, service connection, military history, family history, service utilization, and history of common mood disorders, anxiety disorders, certain medical conditions, substance use disorders, and pharmacological treatment for ADHD.

Methods: Participants will be recruited from outpatient clinics at FHCC. The target enrollment is 290 participants. Inclusion criteria are veterans, age 18-45 years, who can read and understand English, enrolled in FHCC outpatient clinics, and who are cognitively intact. Subjects will be excluded if they are not veterans, cannot both read and understand English, are acutely medically ill, or display current intoxication, altered mental status, or acute psychosis. Participants will complete the ADHD Self-Report Scale (ASRS) v1.1 Symptom Checklist-Expanded, which results in a positive or negative screen for ADHD. A retrospective chart review will obtain secondary outcome measures.
For objective 1: n and % of subjects with ADHD-like presentation will be reported.
For objective 2: descriptive statistics will be used to report correlation of ADHD symptoms with secondary outcome measures

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J Psychiatr Res. 2017;90:110-17.

AGE-DEPENDENT ROLE OF PRE- AND PERINATAL FACTORS IN INTERACTION WITH GENES ON ADHD SYMPTOMS ACROSS ADOLESCENCE.

Brinksma DM, Hoekstra PJ, van den Hoofdakker B, et al.

Little is known about the effects of risk factors on attention-deficit/hyperactivity disorder (ADHD) symptom over time. Here, we longitudinally studied the role of candidate genes, pre- and perinatal factors, and their interactions on ADHD symptoms between ages 10 and 18 years. Subjects were part of the general population or clinic-referred cohort of the TRacking Adolescents' Individual Lives Survey (n = 1667). At mean ages of 11.1 (T1), 13.4 (T2), and 16.2 years (T3), ADHD symptoms were assessed with the Child Behavior Checklist. Linear Mixed Models were used to examine the association of candidate genes (i.e., DRD4, DRD2, 5-HTTLPR, COMT, and MAOA), pre- and perinatal factors (i.e., index measure of various pregnancy and delivery complications, maternal smoking, maternal drinking, and low birth weight), and their interactions with ADHD symptoms across adolescence. Pregnancy and delivery complications were associated with a higher level of ADHD symptoms across all time points, but with a significantly declining influence over time ($p = 0.006$). We found no main effects of the candidate genes on ADHD symptoms throughout adolescence. The simultaneous presence of the low activity MAOA genotype and low birth weight ($p < 0.001$) and of the 5-HTTLPR LL-allele and respectively pregnancy and delivery complications ($p = 0.04$) and maternal smoking ($p = 0.04$) were associated with more ADHD symptoms particularly during early adolescence, and these influences significantly decreased over time. Findings suggest an age-dependent role of gene-environment interactions on ADHD symptoms across adolescence

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J Psychiatry Neurosci. 2017 Mar;42:103-12.

CORTICAL MORPHOLOGY AS A SHARED NEUROBIOLOGICAL SUBSTRATE OF ATTENTION-DEFICIT/HYPERACTIVITY SYMPTOMS AND EXECUTIVE FUNCTIONING: A POPULATION-BASED PEDIATRIC NEUROIMAGING STUDY.

Mous SE, White T, Muetzel RL, et al.

Background: Attention-deficit/hyperactivity symptoms have repeatedly been associated with poor cognitive functioning. Genetic studies have demonstrated a shared etiology of attention-deficit/hyperactivity disorder (ADHD) and cognitive ability, suggesting a common underlying neurobiology of ADHD and cognition. Further, neuroimaging studies suggest that altered cortical development is related to ADHD. In a large population-based sample we investigated whether cortical morphology, as a potential neurobiological substrate, underlies the association between attention-deficit/hyperactivity symptoms and cognitive problems.
Methods: The sample consisted of school-aged children with data on attention-deficit/hyperactivity symptoms, cognitive functioning and structural imaging. First, we investigated the association between attentiondeficit/ hyperactivity symptoms and different domains of cognition. Next, we identified cortical correlates of attention-deficit/hyperactivity symptoms and related cognitive domains. Finally, we studied the role of cortical thickness and gyrification in the behavior cognition associations.
Results: We included 776 children in our analyses. We found that attention-deficit/hyperactivity symptoms were associated specifically with problems in attention and executive functioning (EF; b = 0.041, 95%

confidence interval [CI] 0.07 to 0.01, p = 0.004). Cortical thickness and gyrification were associated with both attention-deficit/hyperactivity symptoms and EF in brain regions that have been previously implicated in ADHD. This partly explained the association between attention-deficit/hyperactivity symptoms and EF (bindirect = 0.008, bias-corrected 95% CI 0.018 to 0.001).
Limitations: The nature of our study did not allow us to draw inferences regarding temporal associations; longitudinal studies are needed for clarification. Conclusion: In a large, population-based sample of children, we identified a shared cortical morphology underlying attention-deficit/hyperactivity symptoms and EF

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J Psychiatry Neurosci. 2017 Mar;42:113-21.

EFFECTS OF DOPAMINERGIC GENES, PRENATAL ADVERSITIES, AND THEIR INTERACTION ON ATTENTION-DEFICIT/HYPERACTIVITY DISORDER AND NEURAL CORRELATES OF RESPONSE INHIBITION.

van der Meer D, Hartman CA, van Rooij D, et al.

Background: Attention-deficit/hyperactivity disorder (ADHD) is often accompanied by impaired response inhibition; both have been associated with aberrant dopamine signalling. Given that prenatal exposure to alcohol or smoking is known to affect dopamine-rich brain regions, we hypothesized that individuals carrying the ADHD risk alleles of the dopamine receptor D4 (DRD4) and dopamine transporter (DAT1) genes may be especially sensitive to their effects.
Methods: Functional MRI data, information on prenatal adversities and genetic data were available for 239 adolescents and young adults participating in the multicentre ADHD cohort study NeuroIMAGE (average age 17.3 yr). We analyzed the effects of DRD4 and DAT1, prenatal exposure to alcohol and smoking and their interactions on ADHD severity, response inhibition and neural activity.
Results: We found no significant gene × environment interaction effects. We did find that the DRD4 7-repeat allele was associated with less superior frontal and parietal brain activity and with greater activity in the frontal pole and occipital cortex. Prenatal exposure to smoking was also associated with lower superior frontal activity, but with greater activity in the parietal lobe. Further, those exposed to alcohol had more activity in the lateral orbitofrontal cortex, and the DAT1 risk variant was associated with lower cerebellar activity. Limitations: Retrospective reports of maternal substance use and the cross-sectional study design restrict causal inference.
Conclusion: While we found no evidence of gene × environment interactions, the risk factors under investigation influenced activity of brain regions associated with response inhibition, suggesting they may add to problems with inhibiting behavior

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J Psychoeduc Assess. 2017 Feb;35:124-37.

DO THE KINDS OF ACHIEVEMENT ERRORS MADE BY STUDENTS DIAGNOSED WITH ADHD VARY AS A FUNCTION OF THEIR READING ABILITY?

Pagirsky MS, Koriakin TA, Avitia M, et al.

A large body of research has documented the relationship between attention-deficit hyperactivity disorder (ADHD) and reading difficulties in children; however, there have been no studies to date that have examined errors made by students with ADHD and reading difficulties. The present study sought to determine whether the kinds of achievement errors made by students diagnosed with ADHD vary as a function of their reading ability. The participants in this study were 91 students in the ADHD clinical validity standardization sample of the Kaufman Test of Educational Achievement' Third Edition (KTEA-3), as well as a control group of 63 students selected from the larger standardization sample. Students with ADHD and reading difficulties demonstrated a statistically significant greater amount of errors across tests of academic achievement. Findings from the study are discussed within the context of past research, as well as implications for the field of school psychology and practitioners

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J Psychopathol Behav Assess. 2017;1-19.

DELIVERING PARENT-TEEN THERAPY FOR ADHD THROUGH VIDEOCONFERENCING: A PRELIMINARY INVESTIGATION.

Sibley MH, Comer JS, Gonzalez J .

Adolescents with ADHD demonstrate notoriously poor treatment utilization. Barriers to access have been partially addressed through tailored therapy content and therapist delivery style; yet, additional challenges to engaging this population remain. To leverage modern technology in support of this aim, the current study investigates parent-teen therapy for ADHD delivered over a videoconferencing format. In this preliminary feasibility study, teens and parents (N = 20) received an empirically supported dyadic therapy that incorporates skills-based modules with motivational interviewing. The videoconferencing interface was deemed feasible with nearly all families completing treatment. Acceptable therapeutic alliance was reported and key mechanisms of change were engaged (i.e., adolescent motivation to meet goals, parent strategy implementation). Families reported high satisfaction, despite minor disturbances associated with delivering therapy via videoconferencing. Treatment integrity and fidelity were acceptable, though slightly reduced compared to clinic-based trials of the same protocol. Therapists perceived that videoconferencing enhanced treatment for 50% of families. Reductions in participant ADHD symptoms and organization, time management, and planning problems from baseline to post-treatment were noted by parents and teachers. However, open trial results of this study should be interpreted with caution due to their uncontrolled and preliminary nature

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J Psychopathol Behav Assess. 2017;39:92-102.

THE FACTOR STRUCTURE OF ADHD-DIFFERENT MODELS, ANALYSES AND INFORMANTS IN A BIFACTOR FRAMEWORK.

Rodenacker K, Hautmann C, et al.

The methodological approach of exploratory structural equation modelling (ESEM) has only been applied once to the construct of Attention-deficit/hyperactivity disorder (ADHD). We decided to compare bifactor models based on confirmatory factor analyses (Bi-CFA) and exploratory equation modeling (Bi-ESEM) only, as there is a growing support of a bifactor structure of ADHD. To examine the factorial validity of the construct we compared three possible bifactor models. One model with two specific factors (inattention and hyperactivity/impulsivity), another model with three specific factors (inattention, hyperactivity and impulsivity) and an alternative, incomplete model with one general ADHD and two specific factors (inattention and impulsivity). We used parent- (*N* = 1386; Age: M = 11.70, SD = 3.18; Sex: 74.5 % male) and teacher-ratings (*N* = 110; Age: M = 11.27, SD = 3.04; Sex: 77.5 % male) from clinically referred children between the age of 6 and 18. The results indicate that both methods lead to equally good model fit and for both informants the reliable variance of the specific factor hyperactivity is almost completely explained by the general factor. However, in the teacher condition cross-loadings seem to be of particular importance. Across both methods and informants covariation among ADHD symptom items can be in most part attributed to a general ADHD factor as well as to three (inattention, hyperactivity and impulsivity) or two (inattention and impulsivity) weakly defined specific factors. Further research regarding associations between the specific factors of ADHD and other disorders (e.g. conduct disorder) should be conducted

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J Can Acad Child Adolesc Psychiatry. 2017;26:31-38.

IS EMOTION RECOGNITION RELATED TO CORE SYMPTOMS OF CHILDHOOD ADHD?

Tehrani-Doost M, Noorazar G, Shahrivar Z, et al.

Objective: Children with attention deficit/hyperactivity disorder (ADHD) have some problems in social relationships which may be related to their deficit in recognizing emotional expressions. It is not clear if the deficit in emotion recognition is secondary to core symptoms of ADHD or can be considered as an independent symptom. This study aimed to evaluate the ability of detecting emotional faces and its relation to inattention and hyperactivity-impulsivity in children with ADHD compared to a typically developing (TD) group.

Methods: Twenty-eight boys diagnosed as having ADHD, aged from seven to 12 years old were compared to 27 TD boys using a computerized Facial Emotion Recognition Task (FERT). Conners' Parent Rating Scale (CPRS) and Continuous Performance Test II (CPT II) were also administered to assess the severity of inattention and impulsivity.
Results: The percentages of angry, happy and sad faces detected by children with ADHD were significantly lower ($p<0.05$) compared to the control group. The time spent in recognizing happy faces was higher in the ADHD group ($p=0.04$). The sequential regression analyses showed a significant association between angry and sad targets recognition and inattention ($P<0.05$), as well as between oppositionality and angry faces detection ($P<0.05$) when hyperactivity-impulsivity was added to the model.
Conclusion: It can be concluded that children with ADHD suffer from some impairments in recognizing angry, happy and sad faces. This deficit may be related to inattention and hyperactivity-impulsivity

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J Can Acad Child Adolesc Psychiatry. 2017;26:21-30.

ATTENTION AND EXECUTIVE FUNCTION IN CHILDREN DIAGNOSED WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER AND COMORBID DISORDERS.

Ter-Stepanian M, Grizenko N, Cornish K, et al.

Objective: The goal of this study was to examine the relationship between comorbid disorders and executive function (EF) in children diagnosed with Attention eficit/Hyperactivity Disorder (ADHD).
Methods: Three hundred and fifty-five, 6-12 year old children clinically diagnosed with ADHD were included in the study. Comorbid anxiety disorders, Oppositional Defiant Disorder (ODD) and Conduct Disorder (CD) were examined. The EF domains were assessed using the Conners' Continuous Performance Test (CPT), Wisconsin Card Sorting Test (WCST), Tower of London (ToL), Finger Windows (FW) and Self Ordered Pointing Test (SOPT).
Results: The findings indicate that children with comorbid anxiety disorders performed worse in domains measured by CPT and prior to controlling for age and sex, by FW. However, once sex was controlled for the results for FW were no longer significant. Children with CD obtained lower scores on WCST. Furthermore, a significant sex by CD interaction was observed.
Conclusion: These results indicate that comorbid disorders should be carefully examined as they play a significant role in EF performance and subsequently in day-to-day functioning of children with ADHD

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J Formos Med Assoc. 2017.

DIFFERENTIAL NEUROPSYCHOLOGICAL FUNCTIONING BETWEEN ADOLESCENTS WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER WITH AND WITHOUT CONDUCT DISORDER.

Lin YJ, Gau SSF.

Background/Purpose: This study aimed to evaluate neuropsychological functioning of attention-deficit/hyperactivity disorder (ADHD) with and without comorbidities of oppositional defiant disorder (ODD) and/or conduct disorder (CD) and the mediation effects of the neuropsychological functions in the relationship between ADHD and ODD/CD symptoms to increase our understanding about these frequently co-occurring disorders.
Methods: Adolescents aged 11-18 years were interviewed by the Kiddie epidemiologic version of the Schedule for Affective Disorders and Schizophrenia to confirm their previous and current ADHD status and other psychiatric diagnoses. The performance of the Cambridge Neuropsychological Testing Automated Battery was compared among four groups: (1) ADHD with CD (ADHD+CD), regardless of ODD; (2) ADHD with ODD (ADHD+ODD) without CD; (3) ADHD without ODD/CD (ADHD-only); and (4) typically developing controls. Mediation effects of neuropsychological functioning were tested.
Results: All three ADHD groups had impaired spatial working memory and short-term memory. Deficits in verbal memory and response inhibition were found in ADHD+ODD, but not in ADHD-only. ADHD+CD did not differ from typically developing controls in verbal working memory, signal detectability, and response

inhibition. Spatial working memory partially mediated the association between ADHD and CD symptoms and alerting/signal detectability of arousal partially mediated the association between ADHD and ODD symptoms. **Conclusion**: There were both common and distinct neuropsychological deficits between adolescents with ADHD who developed ODD only and who developed CD. ADHD comorbid with CD may be a different disease entity and needs different treatment strategies in addition to treating ADHD, while ADHD+ODD may be a severe form of ADHD and warrants intensive treatment for ADHD symptoms

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Kindheit und Entwicklung: Zeitschrift fÃ¼r Klinische Kinderpsychologie. 2017;26:39-47.

VERLAUF EXEKUTIVER FUNKTIONEN BEI VORSCHULKINDERN MIT ENTWICKLUNGSAUFFÃ¤LLIGKEITEN. ADHS-SYMPTOME, SPEZIFISCHE SPRACHENTWICKLUNGSSCHWIERIGKEITEN UND NIEDRIGE INTELLIGENZ. = DEVELOPMENT OF EXECUTIVE FUNCTIONING IN PRESCHOOLERS WITH DEVELOPMENTAL DISORDERS: ADHS SYMPTOMS, SPECIFIC LANGUAGE IMPAIRMENT, AND INTELLECTUAL DISABILITIES.

Schuchardt K, Piekny J, MÃ¤hler C.

Children with specific language impairments (SLI), children with intellectual disabilities (ID), and those with attention deficit hyperactivity disorder (ADHD) symptoms usually have difficulties in executive functioning. The focus of the present study was on investigating children with specific and isolated developmental disorders without comorbid diagnoses. The aim of the study was to find out if children with specific developmental disorders show typical and definable abnormalities in executive functioning, and if the development of executive functioning follows the same or a different developmental course compared with typically developing children. On the basis of the executive functioning model by Miyake et al. (2000), we first investigated children's abilities in Updating, Shifting, and Inhibition tasks. Second, we analyzed whether the preschool teachers reported any problems in self-regulation. We studied 22 children with ADHD symptoms, 24 children with SLI, and 24 children with ID, together with a control group of 35 typically developing children using a longitudinal design. We tested the children's executive functioning at ages 5 and 6 years using the following instruments: Updating: Wordspan backwards, Complex span; Inhibition: Head-Toes-Knees-Shoulders Task (HTKS); Shifting: Dimensional Change Card Sort Test (DCCS). Children's self-regulation was rated by their preschool teachers right before school entry using a questionnaire. Our results showed that some abnormalities in executive functioning overlap between the groups of children with developmental disorders, but there are also definable and specific patterns of abnormalities for every specific disorder. While children with ID have a specific deficit in Updating, children with ADHD symptoms have problems predominantly in the Inhibition and Shifting component of executive functioning. Children with SLI showed the most problems in the Shifting component. The preschool teachers only rated the self-regulation abilities of ADHD children as deficient. Our results indicate that a deficit in executive functioning does not necessarily manifest itself as overt behavior in all children. Therefore, deficits in executive functioning should be examined by measurements of executive performance. The relevance of our results for diagnostics and interventions for children with executive functioning deficits are discussed

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Klin Psikofarmakol Bul. 2016;26:S166-S167.

THE RELATIONSHIP BETWEEN MATERNAL IMPULSIVITY STATE AND SYMPTOM VARIABILITY AND SEVERITY OF CHILDREN WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER.

Tulaci OD, Durukan I, Karaman D, et al.

OBJECTIVE: Attention Deficit Hyperactivity Disorder (ADHD) is one of the most common neurodevelopmental disorder in childhood that is characterized with attention, hyperactivity and impulsivity. Twin and adoption studies showed thar heritability of ADHD is around 60-90%. The aim of this study was to examine whether maternal impulsivity was associated with symptom varibility and severity of children with ADHD.

METHOD: The study sample consisited of 37 male children diagnosed ADHD-mixt subtype according to DSM-IV-TR and their biological mothers. In order to assess the symptom variability and severity of ADHD, the Conner's Teacher Rating Scale/ Revised Long Form, the Conner's Parent Rating Scale/ Revised Long

Form, the DSM-IV Based Screening and Rating Scale for Children and Adolescents with Attention Deficit and Disruptive Behavior Disorders were used. To evaluate maternal impulsivity Adult Self Report Scale (ASRS), and Barratt Impulsivity Scale were used and researchers administered mothers Iowa Gambling Task (IGT), Cued Go/ No-go Task, and Structured Clinical Interview for DSM-IV Clinical Version.
RESULTS: No significiant correlations were found between ASRS points of mothers and the tasks used to evaluate ADHD symptom variability and severity of children with ADHD. There was also no significiant correlation between IGT points of mothers and the tasks evaluating ADHD symptoms of children in the study group. There was a negative correlation between mean reaction time in cued Go/ No-go task of mothers and oppositinal defiance scale points of children. Presence of old major depression and generalized anxiety disorders in mothers did not cause statistically significiant difference in symptom pattern and severity in children with ADHD. We determined that as mothers' mean reaction time increases, children's ADHD symptom severity decreases for mother's assessment. The study also suggests that maternal impulsivity is associated with children's ADHD symptom variability and severity.
CONCLUSION: Including fathers, sisters, and brothers of children with ADHD to this study would help us to understand the effects of familial genetic transmission better in ADHD. The boundaries of impulsivity should be determined better. These findings need to be supported with further studies using larger samples

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Klin Psikofarmakol Bul. 2016;26:S73-S74.

EMOTION RECOGNITION AND THEORY OF MIND DEFICITS IN CHILDREN WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER.

Bolat N, Eyuboglu D, Eyuboglu M, et al.

OBJECTIVE: Children who were diagnosed with attention deficit hyperactivity disorder (ADHD) appeared to represent insufficient social behaviors. This may manifest as rejection by peers and interpersonal discord with other children and adults. Emotion recognition and theory of mind (ToM) abilities are important domains of social cognition. Some authors have reported difficulties in empathy and ToM in children with ADHD. However, several studies did not find any significant difference between ADHD children and control group on the ToM abilities. The aim of this present study was to assess the emotion recognition and theory of mind abilities of children with ADHD.
METHODS: Sixty-nine patients diagnosed with ADHD (48 male and 21 female subjects, with a mean age of 10.03±1.83 years, range 8-15 years) and 69 typically developing children (matched for age and gender; 48 male and 21 male subjects, with a mean age of 10.13±1.96 years, range 8-15 years, without psychiatric or neurological disorder or pharmacological treatment) participated in this study. A semistructured psychiatric interview (Kiddie-schedule for affective disorders and schizophrenia-present and lifetime version) was administered in both groups. The study and control group compared on theory of mind tasks and emotion recognition tests. The statistical analyses were performed using SPSS Version 16.0 for Windows . Chi-square, Mann-Whitney U and Spearman's correlation tests were used to analyze the data. A p value <0.05 was considered to indicate statistical significance.
RESULTS: Regarding the first order ToM task scores, second order ToM task scores and total scores of ToM task, ADHD group have significantly lower scores compared to the controls ($p<0.001$). Moreover, cases in the study group performed poorly on comprehension test and unexpected outcomes test ($p<0.001$). The findings showed positive correlation between total ToM scores and unexpected outcomes scores ($r=0.39$, $p=0.001$), unexpected outcomes scores and comprehension test scores ($r=0.40$, $p=0.001$) in the study group.
CONCLUSIONS: Our results indicate that ADHD seem to have a negative impact on emotion recognition and theory of mind abilities. The findings support the importance of assessing emotion recognition and ToM abilities of children and adolescents with ADHD. Successful social interaction is critically dependent upon our ability to understand other people's mind and their feelings. Impaired interpersonal relationships may be of crucial importance for the prognosis of children with ADHD on both short and long-term. Our results emphasized the potential role of emotion recognition and ToM deficits on inadequate social behaviors of

children and adolescents with ADHD. These findings suggested that there was a need for developing new treatment modalities on emotion recognition and ToM deficits which could provide more positive outcomes in ADHD patients

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Klin Psikofarmakol Bul. 2016;26:S36.

PERCEIVED EXPRESSED EMOTION AND SELF-ESTEEM IN ADOLESCENTS WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER.

Ucar HN, Eray S, Vural P .

OBJECTIVE: Attention deficit hyperactivity disorder (ADHD) is a neurodevelopmental disorder characterized with a persistent pattern of inattention and/or hyperactivity-impulsivity that interferes with functioning or development. ADHD causes serious social, academic and psychological deficiencies in all stages of child and adolescent development. These deficiencies may result in deterioration in interpersonal relations and relations within the family. The study aims at discussing self-esteem and perceived expressed emotion in adolescents with the ages of 12-16 who are diagnosed with ADHD.

METHODS: Included in the study are 41 cases who are diagnosed with ADHD (according to DSM-IV) after the clinical interviews carried out by a child psychiatrist on individuals who presented to Uludag University Medical School Child and Psychiatry Outpatient Clinic in the time period between April 1st, 2015 and July 1st, 2015. Their parents are also included in the study. The control group consists of students from schools run by Bursa Provincial Directorate for National Education who are matched with the sample group in terms of age and gender, presented voluntarily, are not diagnosed with any physical or mental disorder and directed to our outpatient clinic by the psychological counseling and guidance divisions of respective schools. Criteria for exclusion from both groups are determined as the following: uneducated parents, inadequate mental capacity to fulfill the scale and presence of any medical illnesses such as accompanying epilepsy. Adolescents whose total intelligence segment points are equal or above 85 according to the Revised Wechsler Intelligence Scale for Children (WISC-R) form are included in the study. 41 adolescents with ADHD diagnosis and their parents were examined and matched 35 adolescents who as control group and their parents. Schedule for Affective Disorders and Schizophrenia for School-Age Children, Present and Lifetime Version (K-SADS-PL) Turkish Version, Rosenberg Self-Esteem Scale, Shortened Level of Expressed Emotion Scale (SLEES), and WISC-R are used.

RESULTS: In order to analyze the hypothesis ΓÇ£the level of self esteem in adolescents with ADHD is different from their peers, the middle and low self-esteemed individuals and high self-esteemed individuals are sub-grouped as non high self-esteemed and ΓÇ£high selfesteemed respectively. Then, the groups are compared to each other in terms of the distribution of these variables in them. That the 46.3% of the adolescents in the sample group have non-high self-esteem level is statistically significant when compared to the control group. Means of the SLEES by groups were: X=63.2, SD=15.3 for the patient group and X=53.9, SD=12.3 for the control group. There were significant differences in the perceived express emotion scores by groups (t=2.900) (p=0.005). And there were also significant differences in the subscale of SLEES scores by groups.

CONCLUSIONS: The results of this study suggest that self-esteem in the adolescents with ADHD is significantly low and that their perceived expressed emotion is significantly high. This is noticeable for it draws attention to the psycho-social dimension in the clinical evaluation of the children with ADHD

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Klin Psikofarmakol Bul. 2016;26:S127-S128.

COGNITIVE COMPUTER TRAINING IN CHILDREN WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER.

Bozkurt S, Kocas S, Kaya I, et al.

OBJECTIVE: Attention deficit hyperactivity disorder (ADHD) symptoms can be difficult to treat. Pharmacological treatment is commonly used to reduce ADHD symptoms. Whereas, non-pharmacologic treatment methods would be preferred by parents, children and psychiatrists in some cases. Recently, several trials have shown promising results for cognitive computer training. Children with ADHD have a

variety of cognitive dysfunctions, and it is important that cognitive training target multiple cognitive functions. The primary aim of this study is to examine if cognitive computer training would improve attention, executive functions, and working memory in children with ADHD.
METHOD: This study aims to examine the effect of ACTIVATE a computer program designed to improve a range of cognitive skills and ADHD symptoms. A total of 41 children with ADHD, aged 6 to 12 years. The intervention group (n=22) was asked to use ACTIVATE at home 20 minutes 4 days per week for 16 weeks. Ten of them did not use medication for ADHD (Activate Alone). Control group (Medication only n:19) received treatment as usual. Outcome measures assessed cognitive functions and symptoms measures before and after the 8 weeks of training and end of training with NIH Toolbox Tests and conners parent rating scale.
RESULT: The study sample as a whole showed significant improvement on all three tests of cognition following treatment: Reaction Time on Flanker Correct Incongruent trials, $p<0.001$; Percent Correct No-Go trials, $p<0.01$; Working Memory, $p<0.05$. Relative improvement on different tests varied as a function of the type treatment. The Activate alone and the Combined treatment groups showed greater improvement than the Medication only group on the Flanker test of focused attention (373 msec improvement vs. 195 msec). The Medication only and the Combined groups showed greater improvement than the Activate alone group in Working Memory (5.2 points vs. 1.4). However, due to limited sample size and high variability these differences were not significant. The groups showed similar improvement in response inhibition. There was no significant improvement in the conners parent rating scale measures.
CONCLUSION: Few studies have examined the effects of these interventions in children with ADHD, and although these studies generally show promising results (e.g., improvement of ADHD behavior as rated by parents and/ or a significant other, e.g., the teacher; an increase of neural activity and gray matter volume in ADHD affected brain areas), none of these studies are placebo-controlled. To date, most evidence has been found for the trainability of WM. Our study also supports this evidence. 'Cognitive computer training ' is not to be considered a stand-alone treatment module, but one that should be added, combined, or integrated with existing, empirically supported treatments for ADHD, to fully have its therapeutic impact

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Klin Psikofarmakol Bul. 2016;26:S87.

SCHOOL BASED COMBINED EXERCISE AND COMPUTER TRAINING PROGRAM MAY IMPROVE WORKING MEMORY IN ADHD CHILDREN.

Buber A, Yilanli M, Basay O, et al.

OBJECTIVE: Attention deficit and hyperactivity disorder (ADHD) is one of the most common psychiatric disorders of childhood. Deficits in executive functioning such as paying attention, response inhibition, and working memory are significantly important in ADHD. Stimulant medications are best treatment modality so far even some children come across the serious side effects. Beside of stimulant medication treatment, combination with other treatments, are recommended for ADHD population. Higher ADHD rates needs supportive non-pharmacological community-based interventions for children with ADHD. One of the approaches for supportive therapies are neuroplasticity-based cognitive training programs. Recently, studies have shown that training of the executive functions especially working memory has positive effects for children with ADHD. According the clinical point of view it may be assumed that enhanced executive function especially working memory can cause of positive effects on functioning in daily life and quality of life. In our study, we combined computer-presented and physical exercises program for targeting the core deficits of ADHD population. We aimed to examine the influence of the training program of a computerized training program and physical exercises on cognitive performance, ADHD symptoms, and functional impairments.
METHODS: In the this study, 23 ADHD-diagnosed children and 18 control subjects were evaluated. The study participants were assessed at the Pamukkale University Life Long ADHD Research Center. The ADHD and control group subjects were recruited in children satisfying the following criteria: aged between 7 and 12 years, attending a public school, no history of head injury with unconsciousness, no history of neurological or other serious medical diseases or the constant use of prescribed medications for medical conditions, and no use of stimulants or use of psychotropic medications. For the ADHD subjects, any psychiatric disorder was an exclusion criterion; for the control subjects, presence of any psychiatric disorders was not allowed. Ethical approval was granted and approved by the Pamukkale University Research Ethics Committee in accordance with the Helsinki Declaration. Written informed consents were obtained from parents of the

children both for the ADHD group and TD group. Initially, a semi-structured interview (Kiddie-Schedule for Affective Disorders and Schizophrenia, present and life time version - K-SADS-PL) was administered to parents and children by a child psychiatrist. The same psychiatrist also performed a mental status examination of each child. The group played computer training at school 20 minutes per day, 4 days per week for 10 weeks. Physical exercise was applied at the same day just before the computer program for 40 minutes. Good behavioral game were played during all program to manage of children behaviors that motivate with rewards the children for displaying appropriate behaviors during program.
RESULTS: Initially, a total of 23 ADHD-diagnosed children and 18 control subjects were evaluated with clinical assessments. (Because of the some drop outs and missing pre/post scales or cognitive assessments, final numbers might be different.)
CONCLUSIONS: The influence of the school based combined exercise and computerized training program on cognitive performance, ADHD symptoms, and functional impairment were evaluated. Our findings suggest that school based combined exercise and brain training program has improved the cognitive functions, especially working memory, in children with ADHD. This finding is supported clinically by the improvement in functionality. However a generalized decrease in ADHD symptoms was not found. Future studies with larger samples to distinguish the responders and non-responders as well as to assess long-term effects are needed

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Klin Psikofarmakol Bul. 2016;26:S187-S188.

CARBOXYLESTERASE1, ALPHA 2A ADRENERGIC RECEPTOR AND NORADRENALIN TRANSPORTER GENE POLYMORPHISMS AND THEIR CLINICAL PRESENTATIONS IN ATTENTION DEFICIT HYPERACTIVITY DISORDER.

Cetin FH, Isik Y, Onen HI.

OBJECTIVE: The role of genetic factors in pathogenesis of ADHD is proven in multiple studies. Dopaminergic pathways are studied in detail because of the fact that MPH is a DAT inhibitor. Recently, due to efficient use of ATX in treatment, which is a NET inhibitor, and the definition of noradrenalin's effect on attention functions, researchers are focused more on the adrenergic pathways. Also, after understanding the fact that polymorphisms in the CES1 gene, which codes the carboxylesterase 1 enzyme that breaks down MPH, change the enzyme activity, studies are focused more on the metabolic pathways. The objective of this study was to examine the association between ADHD and G1287A polymorphism in the NET1 gene, C1291G polymorphism in the ADRA2A gene on the adrenergic pathway and Gly143Glu polymorphism in the CES1 gene on the metabolic pathway, and their clinical effects.
METHOD: The study population included 114 patients who presented to the Gazi University Child and Adolescent Psychiatrics Department and are diagnosed with ADHD according to DSM IV-TR and 83 healthy controls aged between 6 and 16. Subsequent were evaluated by clinical examination and Conner's Comprehensive Behavior Rating Scale-Teacher (CRS-T), venous blood sample is taken and gene analysis is made. 103 patients are followed for 6 months (at the 2nd, 4th, and 6th months), their scale points are recorded and side effects are questioned in each interview.
RESULTS: Every patient in both control and ADHD group are found to have GG genotype when Gly143Glu polymorphism in the CES1 gene is examined, thus we came to a conclusion that Turkish population is homozygote in the mentioned polymorphism. No significant association between NET1 gene G1287A polymorphism genotypes and ADHD was found. It was found that ADRA2A C1291G polymorphism C allele and CC genotype is a risk factor for ADHD (p=0.003, OR:2.17, CI:12.8-37.0) and the risk is higher in males (p=0.013, OR:2.43, CI: 12.0-49.5). There was no significant relation between ADRA2A C1291G polymorphism and clinical parameters but it was found that individuals with NET1 G1287A polymorphism AA genotype have less concurrent Oppositional Defiant Disorder diagnosis (18.8% vs. 81.2%, p=0.039), their initial CTRS-attention deficit points are higher (17.47±3.73 vs.16.15±4.58, p=0.045) and their response to treatment is weak according to CTRS-behavior problem points (25.0% vs. %75.0, p=0.023).

CONCLUSION: In conclusion, the present study showed that the ADRA2A C1291G polymorphism C allele and CC genotype is susceptibility factor in the etiology of ADHD. NET1 G1287A polymorphism AA genotype is associated with clinical response to ADHD treatment. Further studies on genetic variants of adrenergic/ metabolic pathways will focus on its role in specific subtypes of ADHD, their response to pharmacotherapy, and also the role of sex effect

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Klin Psikofarmakol Bul. 2016;26:S105.

THE RELATIONSHIP BETWEEN ATTACHMENT AND PARENTING STYLES IN PARENTS OF ADOLESCENTS WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER.

Kinik MF, Gundogdu OY.

OBJECTIVE: Attention deficit and hyperactivity disorder (ADHD) is one of the most commonly occurring psychiatric disorders seen during childhood. Attachment is defined as the lifelong relationship between the child and care-giver; furthermore it is the duration of time when the child forms emotional bonds towards the caregivers. Some studies have postulated that there may be a relationship between insecure attachment and ADHD, and that problems with attachment may contribute towards the development of ADHD. Parenting style shapes family and dictates the socio-emotional development of the child. Caregivers in children with ADHD have been found to be more dismissive and exert more control over the child's own volition when compared to the caregivers of children who do not have ADHD. However, there is lack research in the literature examining examines attachment styles between children or adolescents and their caregivers, and link between parenting styles. In this study we aimed to examine the parenting styles of mothers and the styles of attachment between the care-givers and the adolescents.
METHODS: This study was carried out over a period of three months at the University of Kocaeli University Child Psychiatry Department's ADHD Outpatient Clinic and included adolescents between the ages 13-17. 53 adolescent participants meeting the inclusion criteria were included in both the ADHD and the control group. Both groups were asked to fill the adolescent and maternal self-reported forms followed by diagnostic interviews carried out to screen the presence of chronic physical illness, history of head trauma, non-biological parents, co-morbid psychiatric diagnosis to ADHD. Participants scoring below 80 in the Wechsler scale were excluded. Diagnosis of ADHD of the participants in the study group was made using the K-SADS-PL-T. Adolescents who met the criteria after being assessed by K-SADS-PL-T, also filled out the Socio-demographic Information Form, Relationships Scales Questionnaire (RSQ), and Parental Attitude Research Instrument.
RESULTS: There was no difference in age or gender distribution between the ADHD and control groups. Furthermore, there was no difference between maternal ages of the participants both in the ADHD and control groups. Democratic attitude subscale of RSQ in the control group values were higher than the ADHD group ($p<0.05$). Other subscale scores did not show significance between the two groups. A moderate positive correlation was found between the maternal democratic attitude and maternal secure attachment ($r=0.311$, $p<0.05$). A moderate level of negative correlation was found in maternal fearful attachment style between democratic attitude and equalitarianism scores ($r=-0.316$, $p<0.05$). There was no difference between parental attitudes and adolescent attachment styles.
CONCLUSION: Our study has shown that adolescents with ADHD who compared for secure and insecure attachment styles had no difference between maternal parenting attitudes. In this study as expected, mothers of children with ADHD are more critical and secure attachment style of mother cause more receptive approach to their children

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Klin Psikofarmakol Bul. 2016;26:S120-S121.

THE RELATIONSHIP BETWEEN ATTACHMENT STYLES OF ADHD DIAGNOSED ADOLESCENTS AND THEIR MOTHERS.

Kinik MF, Gundogdu OY.

OBJECTIVE: ADHD is the most common psychiatric disorder in childhood. Some studies have shown an association between insecure attachment and development of ADHD, and it is also attachment problems

contribute to the development of ADHD are reported. In the literature there are limited number of studies examining relationship between ADHD and attachment styles of adolescentes and their mothers. In our study, we aimed to examine the relationship between attachment styles of parents and attachment styles of adolescents diagnosed with ADHD, also the anxiety levels of mother and adolescence and how ADHD diagnosis in adolescence have influences on attachment.
METHODS: This study included adolescents that were being followed in the Kocaeli University Child Psychiatry ADHD outpatient clinic between the ages of 13 and 17 and presented to the pediatric outpatient clinic during a three-month period. The ADHD group consisted of 53 adolescents, and the control group consisted of 53 adolescents. Diagnosis of ADHD of the participants in the study group was made using the K-SADS-PL-T. Adolescents and mothers in the both groups were asked to fill the relationships scales questionnaire, state trait anxiety inventory and also mothers in the both groups were asked to fill social-demographic information form and Weiss functional impairment rating scale-parent report. In the ADHD group, ADHD comorbid psychotic disorders, conduct disorders, anxiety disorders, mood disorders, pervasive developmental disorder, participants scoring below 80 in the Wechsler scale, history of head trauma and presence of chronic physical illness have been exclusion criteria from the study.
RESULTS: No difference was identified between the attachment styles of the adolescents in the ADHD and control groups, or between the attachment styles of their mothers ($p>0.05$). Additionally, when the effect of the mother's attachment style on the adolescent's attachment style was examined, no significant difference was identified between secure and insecure attachment styles among the ADHD and control groups ($p>0.05$). The insecure attachment style was more common among the girls in the ADHD group than it was in the boys ($p<0.05$). No difference was identified between the attachment styles of the adolescents in the ADHD group and their mothers ($p>0.05$). The trait anxiety scores of the insecurely attached adolescents in the ADHD group were higher than the scores of securely attached adolescents ($p>0.05$). In the ADHD group, no difference was identified between the functional impairments of the securely and insecurely attached adolescents. No negative correlation was identified between the mean adolescent secure attachment style scores and mean trait anxiety scores, and no positive correlation was identified between the mean adolescent preoccupied attachment style scores and the trait anxiety scores ($p<0.05$).
CONCLUSION: Unlike the current literature, in our study, it was determined that the distribution of attachment styles is similar among the adolescents in the ADHD group and the control group. Also there was no relationship between the distribution of the attachment styles among the adolescents diagnosed with ADHD and their mothers. It has been concluded that to assess attachment in future studies, semi-structured methods should be used and patients newly diagnosed with ADHD should be evaluated

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THE PREVALENCE AND ASSOCIATED FACTORS OF INTERNET ADDICTION AMONG ADOLESCENTS WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER: THE ASSOCIATIONS WITH SUBTYPES, SYMPTOM DIMENSIONS AND COMORBIDITIES.

Bostan R, Ekinci O.

OBJECTIVE: Attention deficit hyperactivity disorder (ADHD), especially in adolescence, has been known as a risk factor of internet addiction. This study aimed to assess the effects of attention deficit hyperactivity disorder (ADHD) symptom dimensions, subtypes, and comorbidities on Internet addiction (IA) among adolescents.
METHODS: This study consisted of 129 adolescents who were diagnosed with ADHD according to DSM-5 (38 females, 91 males) and 108 healthy controls (42 females, 62 males) who did not have any psychiatric disorders or physical illnesses, ranging from 12 to 18 years of age. Adolescents with ADHD and healthy controls were asked to complete internet addiction scale (IAS) and weekly internet use scale developed by the authors. Adolescents with ADHD also completed the Childhood Depression Inventory (CDI) and State Trait Anxiety Inventory and their parents were asked to complete the Turgay DSM-IV-Based Child and Adolescent Disruptive Behavioral Disorders Screening and Rating Scale (T-DSM-IV-S) as data collection tools. ADHD subtypes, including the restrictive subtype, and the comorbidities including anxiety disorder, major depression, oppositional defiant disorder and conduct disorder were diagnosed with a structured clinical interview based on DSM-IV criteria (SCID-I). In addition to the comparative analyses between study

groups, a multiple regression analyses were performed to determine the predictors of problematic internet use (IAS score above 50) among adolescents with ADHD.
RESULTS: In the ADHD group, the frequencies of internet addiction and risky internet use were 7.8% and 46.5%, respectively. In the healthy control group, the frequency of risky internet use was 14.8% and internet addiction was not detected. Average weekly internet usage time and IAS scores were found to be significantly higher in the ADHD group than the control group. No statistically significant difference was found between the three ADHD subtypes (combined, predominantly inattentive and restrictive) with respect to IAS scores and weekly internet usage. The frequency of conduct disorder, but not the other comorbid diagnoses, were higher in those with a IAS score>50. Pearson's correlation analysis revealed that T-DSM-IV-S, conduct disorder, and Beck depression scores demonstrated significant positive correlations with IAS scores. According to the multiple logistic regression analysis, only the T-DSM-IV-S scores were found as a predictor of problematic internet use among adolescents with ADHD.
CONCLUSIONS: The results of this study showed that problematic internet use is more common in adolescents with ADHD than the healthy controls. Clinicians should screen the possible comorbidities of conduct disorder and depression in those with a problematic internet use. Inattentiveness symptoms, but not the ADHD subtypes, appeared to be a strong predictor of internet addiction

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RELATIONSHIP OF HEMATOLOGICAL VARIABLES AND COMORBIDITY TO SYMPTOM RATINGS OF CHILDREN WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER.

Gul H, Gul A, Solmaz EY.

OBJECTIVE: Attention deficit hyperactivity disorder (ADHD) is a common neuropsychiatric disorder with the mean prevalance of 5.9%. Its etiology is still unclear but most commonly it is considered to develop as a result of interactions between genetic and environmental risk factors. ADHD is also observed with comorbid conditions such as iron and other micronutrient deficiencies, depressive disorders, and learning disabilities. Many hematological variables have been reported as a potential predictor in the etiology and treatment activity of ADHD but thus far, results regarding this issue have been contradictory. Our aim was to examine the relation between behavioral symptoms and hematological variables which are related with iron deficiency, Vitamin B12 deficiency, anemia, ferritin, hemoglobin, mean corpuscular volume (MCV), and reticulocyte distribution width (RDW) in children and adolescents with pure Attention Deficit Hyperactivity Disorder (ADHD) or ADHD comorbid with other psychiatric disorders.
METHOD: The sample consisted of 49 subjects with ADHD, 10 of these subjects had other comorbid conditions. The Schedule for Affective Disorders and Schizophrenia for School Age Children-Present and Lifetime Version was performed in a semi-structured interview during the diagnosis. Conners Parent (CPRS) and Teacher Rating Scales (CTRS) were obtained. Hemogram, serum iron, iron binding capacity, serum ferritin levels, T3, T4, TSH, Vitamin B12 and folate were assessed. Iron deficiency was defined as ferritin < 12 ng/ml or MCV < 70 fL and RDW > 14.5, vitamin B12 was defined as <191, hypotiroidy was defined as TSH < 4.3, T4 < 0.9, T3 < 2.5. Anemia was defined as serum hemoglobin < 11.0 g/dl. All patients were diagnosed for the first time and had never been evaluated for psychiatric disorders or treated with psychotropics.
RESULTS: We found that 6.1% of subjects were hypothyroidic, 34.7%of them had Vitamin B12 deficiency, and 22.4% were anemic. There were no significant differences between the pure ADHD patients and the ADHD and comorbid disorders group in terms of parameters mentioned above. In the ADHD group in general, CPRS and CTRS Total scores were significantly negatively correlated with ferritin and Vitamin B12 levels.
CONCLUSION: To our knowledge, our current study is one of the first studies to compare serum ferritin, T3, T4, TSH, Vitamin B12 and other hematological variables, in ADHD and ADHD and comorbid disorders group. Findings is important for both the etiology, treatment, and clinical views of ADHD

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ADOLESCENT IMPULSIVITY AND ITS RELATIONSHIP WITH PSYCHOPATOLOGY IN A CLINIC SAMPLE.

Gokce S, Yusufoglu C, Ayaz AB, et al.

OBJECTIVE: The impulsive behavior that is defined as lacking cognitive control over behavior, is characteristic of adolescence. Impulsivityis associated with deficits in executive function and often linked to rise in sensation seeking. And it may reflect underlying neurodevelopmental processes and psychopathology. In this study we aimed to assess impulsivity in adolescent psychopathology in a clinic sample.

METHODS: Two hundred and thirty three adolescents who admitted to the Erenkoy Mental Health Research and Training hospital between January, 2015 and March, 2015, were evaluated in this study. Psychiatric diagnosis were made by child and adolescent psychiatrists. Adolescents filled Barret Impulsiveness scale and parents completed SNAP IV ADHD scale.

RESULTS: 50.9% of the participants were female and 49.1% were male. Mean age of girls were 14.7±1.7 (10.8-18.0) and mean age of boys were 14.4±1.7 (11.2-18). 66.7% of the adolescents had Attention Deficit Hyperactivity Disorder diagnosis (45.5% were predominantly inattentive type and 19.7% were predominantly hyperactive type). 19.7% of the sample had major depression, 1.3% had Post Traumatic Stress Disorder, 3.8% had Obsessive Compulsive Disorder, 9% had Anxiety disorder, 12% had Adjustment disorder, 6.8% had Conduct disorder, 3.4% had Oppositional Defiant disorder, and 4.3% had learning disorder. Adolescents who were diagnosed as major depression had increased impulsivity levels according to the Barret impulsivity scale than other diagnosis. Attention Deficit Hyperactivity Symptoms were increased in adolescents with ADHD than other diagnosis according to the SNAP IV ADHD scale.

CONCLUSIONS: Impulsivity is related to several psychopathological states in adolescence. We found an increased impulsivity levels in adolescents with major depressive disorder in our clinical sample. We will discuss comorbid ADHD diagnosis and attention deficit hyperactivity symptom severity levels' relation with impulsivity. Since impulsivity is a multi-dimensional construct, it should be taken into account with its different cognitive, clinical, and behavioral aspects

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THE SOCIODEMOGRAPHIC FEATURES, COMORBID PSYCHIATRIC DIAGNOSIS, AND TREATMENT OF CHILDREN DIAGNOSED ATTENTION DEFICIT AND HYPERACTIVITY DISORDER: A PRELIMINARY STUDY.

Karadeniz S, Karakus M, Kandil S.

OBJECTIVE: Attention deficit and hyperactivity disorder (ADHD) is the most frequent neuropsychiatric disorder in children which causes impairment in psychosocial functioning such as problems in social relationships and academic failures at school. Its prevalence is thought to be 5.9-7.1% in studies made in recent years. In various studies it was reported that additional psychiatric diseases aggravate ADHD's symptoms and affect the response to treatment negatively. The aim of this study was to examine the sociodemographic features, comorbid psychiatric conditions, and treatment in 6-18 years children with ADHD.

METHODS: One hundred and sixty four children and adolescents who were followed-up at the Child and Adolescent Psychiatry Outpatient Clinics of Karadeniz Technical University School of Medicine between 1 January 2014 nad 31 June 2014, diagnosed with ADHD according to DSM-5, and had at least three outpatient visits and did not meet the exclusion criteria are were included in this study.

RESULTS: It was found that 120 (73.2%) of the 164 ADHD patients are boys and 44 (26.8%) of them are girls. 69 (42.1%) of these patients are attention deficiency (AD) subtype of ADHD (ADHD group A), 81(49.4%) of them are combined subtype of ADHD (ADHD group C) and 14 (8.5%) of them are hyperactivity-impulsivity predominant subtype of ADHD (ADHD group H). The mean age of ADHD-A group is 10±3.020, ADHD-C group is 9.05±2.484 and ADHD-H group is 8.71±2.091. If we examine for the comorbid psychiatric diagnosis, the ratio of having at least one comorbid psychiatric conditions is 75.6% (124). 42% (69) of the patients have one comorbid condition with ADHD, 31.7% (52) of the patients have two comorbid conditions with ADHD and 1.8% of the patients have three comorbid conditions with ADHD. 24.4% of the sample have no psychiatric comorbid condition. Oppositional defiant disorder is the most frequent psychiatric comorbid condition overall the sample. It is the comorbid condition in 43 (26.2%) patients. In 41(25%) patients behavioral disorders, in

36 (22%) patients anxiety disorder, in 22 (13.4%) patients nocturnal enuresis, in 17 (10.4%) patients tic disorders and in 10 (6.1%) patients depressive disorder is the comorbid condition. In our sample 164 of the patients have a treatment for ADHD. 107 (65.3%) of these patients use long-acting methylphenidate, 33 (20.1%) of these patients use short-acting methylphenidate, 14 (8.5%) of them use atomoxetine for ADHD treatment. 10 (6.1%) patients have no treatment.
CONCLUSIONS: Children with the ADHD accompanied with comorbid psychiatric conditions are possibly more resistant to treatments. In these patients both ADHD and comorbid psychiatric conditions must be treated effectively. The higher ratio of comorbid conditions in our study sample suggests that both diagnosis must be treated

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EFFICIENCY AND SIDE EFFECT PROFILE OF LONG ACTING METHYLPHENIDATE: CASE SERIES IN NATURAL CLINIC SETTING.

Kayis H, Ozbaran NB, Kose SG, et al.

OBJECTIVE: Attention deficit hyperactivity disorder (ADHD) is a heterogeneous neurodevolopmental disorder affecting approximately 5% of children worldwide that is characterized by the core symptoms of difficulty in regulating attention, general motor restlessness, and lack of control of impulses. Academic failure, and troublesome peer and family relationships are associated with ADHD and patients are often diagnosed with one or more co-morbid psychiatric disorders. There are several medication options that have proved efficacy on ADHD symptoms as well as co-morbid conditions. Methylphenidate is the most frequently used and best studied medication in ADHD treatment. Owing to the short half-life and the issues associated with multiple daily dosing of immediate-release MPH formulations, longacting MPH formulations has emerged. Worldwide different kind of long-acting MPH formulations are available in different regions and countries. These long-acting MPH formulations vary according to their modified-release technology, immediate-release (IR): modifiedrelease (MR) ratios and duration of actions. There were just two kind of MPH formulation in Turkey, short-acting/ immediate-release (Ritalin) and long-acting/ modified-release (Concerta) which is using OROS (Osmotic Release Oral System) modified-release technology with 22 to 78% ratio of immediate-release: extended-release MPH and 12 hours duraion of action. Recently new long-acting MPH preparation (Medikinet Retard) started marketing in Turkey. Medikinet retard contains equal proportions of IR and MR MPH. This once daily extended-release formulation have a duration of action about 8 hours with efficacy corresponding to twice-daily administration of IR MPH. Dopfner et al. claimed in their clinical trial that Medikinet retard with a higher IR component than Concerta and an equivalent daily dose is superior to Concerta in the morning and that children and adolescents may also be treated with a lower daily dose of Medikinet retard without resulting in a clinically relevant adverse effects during school time. The objective of this naturalistic study was to examine efficacy and side effect profile of Medikinet Retard in our outpatient clinic patients previously on other MPH preparations and needed to change Medikinet Retard for different reasons.
METHOD: As prelaminary data: At Ege University Department of Child and Adolescent Psychiatry outpatient clinic, 163 patient with ADHD were screened in a natural settings in three months (n=163). %8 of screened patient are treated with Medikinet Retard as second or third choise (n=13).
RESULTS: Mean CGIS-S score before medikinet therapy (while using other methylphenidate therapy) was 3.46, mean CGIS-S score after the medikinet therapy was 2,46. The most common side effects were appetite reduction (n=3, 23.07%), retardation (n=2, 15.3%), irritability (n=1, 7.6%), dizziness (n=1, 7.6%).
CONCLUSION: It is demonstrated that a carefully monitored and titrated stimulant therapy reduces not only the core symptoms but also the associated behavioral problems while increasing psychosocial functioning in ADHD patients. Due to the different pharmacokinetic profiles of the various MR MPH products, different time courses of action throughout the day are expected and this might be significant for some patients with regards to side effects and efficacy. Pharmacokineticly different preparation of methylphenidate may help coping with side effects and better efficacy

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RELATIONSHIP OF THE ATTENTION DEFICIT AND HYPERACTIVITY DISORDER AND BIRTH ORDER.

Yurumez E, Ugur C.

OBJECTIVE: The purpose of this study is to examine the relation between birth order, number of siblings, and prevalence of Attention Deficit Hyperactivity Disorder (ADHD), among boys and girls born by vaginal delivery.

METHODS: Sixty six children with ADHD and 77 healthy children were included. Diagnoses were made using criteria from the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5), based on face-to-face interviews with the children and their parents. The Turgay DSM-IV-Based Child and Adolescent Disruptive Behavioral Disorders Screening and Rating Scale (T-DSM-IV-S) was completed by parents, and sociodemographic features were assessed. Participants were also administered the Schedule for Affective Disorders and Schizophrenia. The ADHD children's scores were compared with those of the control group.

RESULTS: The ADHD children had between 1 and 4 siblings. 43 (65.2%) of them were the first child in their family, 20 (30.3%) were the second child, 2 (3%) were the third child, and 1 (1.5%) of them was the fourth child. In the control group, the children had between 1 and 3 siblings. 48 (62.3%) of the 77 healthy children were the first in their family, 24 (31.2%) were second, and 5 (6.5%) were third. The birth order of the two groups was not significantly different. Likewise, there was no significant difference between the two groups in terms of gender and scores on the scale. However, the number of siblings was correlated to the hyperactivity-impulsivity subscale scores of the ADHD scale.

CONCLUSIONS: This study examined several aspects of the relationship between ADHD and birth order. In order to contribute in this area, we aimed to compare the birth order and number of siblings in a group of ADHD children vs. a control group. It is clear that further studies on birth order and family structure are needed, as ADHD has a lot of unknown and varied etiological factors

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TEMPERAMENT CHARACTERISTICS IN ATTENTION DEFICIT AND HYPERACTIVITY DISORDER.

Mart M, Kenar ANI.

OBJECTIVE: Attention Deficit Hyperactivity Disorder (ADHD) is a chronic, developmental psychiatric disorder beginning in childhood and continuing into adulthood with symptoms of inattention, impulsivity, and hyperactivity. In addition, ADHD patients often experience emotional problems, such as irritability, irritable temper, frequent shifts in mood, and difficulties in regulating behaviour in response to emotional activation. There is no much studies based on the affective temperamental characteristics of adults diagnosed with ADHD. The aim of this study was to determine if adults diagnosed with ADHD would show any specific temperamental characteristics when compared to the healty controls.

METHODS: We recruited 49 outpatients with ADHD from psychiatry clinic of the Pamukkale University (age range 16 and 65 years old). Participants were diagnosed DSM-IV-TR criteria using the Structured Clinical Interview for DSM-IV Axis-I Disorders (SCID-I). We enrolled 40 healthy controls matched for age and education level, with an age between 18 and 65 years, without a history of any mental disorders or neurological disease. All participants completed Wender-Utah Rating Scale (WURS), The Temperament Evaluation of Memphis, Pisa, Paris and San Diego-Auto questionnaire (TEMPS-A) and Adult Attention Deficit Hyperactivity Disorder Diagnosis and Evaluation Scale. Adults for Attention Deficit Hyperactivity Disorder with a subset of 25 questions associated with that diagnosis. Wender-Utah Rating Scale (WURS) was developed by Ward and Wender in 1993. Adult ADD/ADHD DSM IV-Based Diagnostic Screening and Rating Scale Adult Attention Deficit Hyperactivity Disorder Diagnosis and Evaluation Scale were developed by Turgay in 1995. The TEMPS-A developed by Akiskal et al. is a yes-or-no type self-report questionnaire designed to measure affective temperamental traits, present over the course of a person's entire life. The Turkish version inquires about lifelong behavior patterns and consists of 99 items to define 5 temperament subtypes: depressive, hyperthymic, irritable, cyclothymic and anxious.

RESULTS: Patients with ADHD that mean age of 29.04±7.48 years, while control group's was 32.68±8.48. Anxious, irritable, cyclothymic temperament scores were statistically significantly higher in the ADHD group than in the control group (p=0.0001; p=0.0001; p=0.0001, respectively). In group patients of ADHD, irritable temperament compared to the control group was significantly dominant (p=0.043).

CONCLUSION: In this study, our aim was to identify the temperamental characteristics of adults diagnosed with ADHD. The most common dominant temperament was irritable temperament for the ADHD group. In studies conducted previously, it was found results similar to ours. In one study, it was found that in particular were higher in cyclothymic temperament ADHD. These results were indicated to be associated with more childhood and adult ADHD symptoms, lower educational and occupational achievements and increased psychiatric comorbidity. In sum, ADHD group's anxious, irritable, cyclothymic temperament scores is higher than normal population and further research in this field should be continued and the relationship between psychiatric comorbidity and sub-groups of ADHD should be analyzed

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ASSOCIATION BETWEEN PERCEIVED EXPRESSED EMOTION AND PSYCHOPATHOLOGY IN ADOLESCENTS.

Eray S, Vural P, Sigirli D.

OBJECTIVE: Expressed emotion (EE) has an empirically derived definition, which originates from studies of the emotional climate of the family. EE is defined as a prognostic factor in psychiatric disorders. Our purpose was to examine the association between perceived EE and emotional and behavioral problems, attention deficit and hyperactivity (ADHD), peer relationship problems and prosocial behaviors in non-clinical adolescents. Another purpose of our study was to assess the association in non-clinical samples between sociodemographic variables such as age and sex and EE.

METHODS: The research group was composed of high school students who were in continuing studies in 2014-2015 at secondary education institutions in Gebze, Kocaeli. The data were collected using the Information Collection Form, Strengths and Difficulties Questionnaire (SDQ), and Shortened Level of EE Scale (S-LEES).

RESULTS: There were significant positive relationships between the EE and the sub-scales of S-LEES; lack of emotional support, intrusiveness and irritability and the sub-scales of the SDQ; emotional problems ($p<0.001$), behavioral problems ($p<0.001$), ADHD ($p<0.001$), and peer relationship problems ($p<0.001$). There was also a negative significant relationship between prosocial behaviors and EE ($p<0.001$).

CONCLUSIONS: The results of the present study revealed a strong relationship between EE and psychopathology in a non-clinical sample in Turkey. Given the importance of EE in the diagnosis and treatment of preventative mental health and psychopathologies, we believe that the concept of EE in non-clinical samples is useful in preventing disorders and in guiding the treatment of mental disorders. This study is the first investigation of EE and psychopathology in a non-clinical sample in Turkey and first study used a self-report scale which was developed special for adolescents

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THE RELATIONSHIP BETWEEN INTERNET ADDICTION AND DEPRESSION IN ADOLESCENTS WITH ATTENTION DEFICIT AND HYPERACTIVITY DISORDER.

Kahraman O, Durmus TP, Irmak A, et al.

OBJECTIVE: Attention Deficit and Hyperactivity Disorder (ADHD) is one of the most common neurodevelopmental disorders of childhood. Previous research has been shown that ADHD is commonly comorbid with other psychiatric disorders. Depression occurs in adolescents with ADHD at a significantly higher rate than in adolescents without ADHD. The internet is becoming major influences in the lives of adolescents. Internet addiction is a disorder which includes preoccupation with internet and failing in control of internet use that causes impairment in the global functioning of life. Behavioral dys-inhibition, poor neurocognitive skills, and immediate reward preference in children with ADHD have been suggested as risk factors for internet addiction. In addition, various studies have examineexamined the relationship between Internet addiction and the psychological characteristics of adolescents, including depression. In this present study, we aimed to the determine relationship between internet addiction and depression in adolescents with ADHD.

METHODS: One hundred and eleven patients with ADHD whose age range 12 to 18 who were followed up in Erciyes University Medicine Faculty's Child and Adolescent Psychiatry Department were included in this study. The control group consisted of 108 adolescents who has no history of psychiatric disorders by psychiatric interviews. Patients and control groups were asked to complete sociodemographic data form, Internet Addiction Scale (IAS), and Children's Depression Inventory (CDI). Parents of all adolescents were asked to complete Atilla Turgay Scanning and Evaluation Scale based on DSM-IV for Behavioral Disorders in Children and Adolescents.
RESULTS: ADHD group's mean age was 13.9±1.9, control group's mean age was 13.7±1.8 years. There were 29 girls, 82 boys in ADHD group and 30 girls, 78 boys in the control group. There were no significant age and sex differences. The two groups had the similar socioeconomic level. IAS include deprivation, control difficulties, functional impairment, and social isolation subscales. IAS subscales (p=0.007,0.000,0.008,0.000) and total scores (z=-3.814, p=0.000) of adolescents with ADHD were found significantly higher in comparison to the control group. IAS scores correlated significantly with domains of inattention (r=0.406, p<0.001), hyperactivity (r=0.495, p<0.001), and impulsivity (r=0.434, p<0.001) scores. When compared to control group, ADHD group depression scale scores were significantly higher (z=-3.259, p=0.001). IAS and CDI scores were not statistically different between sub-types of ADHD. IAS scores had positive correlation with depression scores in ADHD group (r=0.429, p=0.000) and control group (r=0.549, p=0.000).
CONCLUSION: These results support that ADHD would present as a risk group for internet addiction. Similarly depression scale scores were significantly higher in the ADHD group. This result confirms a relationship between ADHD and depression. The relationship between internet addiction scale scores and depression scale scores are similar in ADHD and control group. Thus, ADHD is thought to be an independent risk factor from depression for internet addiction risk

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RELATIONSHIP BETWEEN ADHD SYMPTOMS AND SLEEP-WAKE CYCLE IN MEDICATION FREE CHILDREN WITH ADHD? A PRELIMINARY STUDY IN TURKISH CHILDREN UNDER TWELVE YEARS OLD.

Tarakcioglu MC, Kadak MT, Gurbuz HGA, et al.

OBJECTIVE: Studies suggest that up to 70% of children with ADHD have sleep problems. The sleep problems reported by parents and children include difficulties in falling asleep and maintaining sleep, tiredness when waking up, daytime sleepiness, bedtime resistance, delayed sleep onset, frequent night waking, frequent motor movements during sleep and morning/ daytime fatigue, snoring, head banging, restlessness, and nighttime awakening problems in ADHD. The aim of our study is to examine the relative contributions of circadian preferences and ADHD symptoms in relation to sleep onset issues, specifically - sleep onset insomnia and bedtime resistance - experienced by children with ADHD.
METHODS: Sleep onset insomnia and bedtime resistance - experienced by children with ADHD (n=53) and in controls (n=38) were recruited into the study. Our hypothesis is that evening preferences among children with ADHD are associated with more inattention. Another important issue of our study was firstly examine circadian preferences of children with ADHD in Turkish population as far as known. Parents completed Conners' Parent Rating Scale-Revised, The Children's Chronotype Questionnaire (CCTQ), and Children's Sleep Habits Questionnaire (CSHQ) to assess sleep variables.
RESULTS: Results indicated that ADHD patients had more sleep onset problems, parasomnias in CSHQ compared to the controls. However, circadian preferences did not differ in CCTQ. Another important finding was mild to moderate correlation between parasomnia, bedtime to sleep in scheduled days, and ADHD symptoms.
CONCLUSION: Our study showed that children with ADHD had more waking-up difficulties and more resistance to bed than controls in school days. However, in contrast to our hypothesis, morningness/ eveningness preference did not differed between ADHD and controls

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THE ADVERSE EFFECTS OF STIMULANT AND NON-STIMULANT MEDICATION TREATMENT OF ATTENTION DEFICIT HYPERACTIVITY DISORDER (ADHD) IN CHILDREN AT A TRAINING HOSPITAL: A RETROSPECTIVE-FOLLOW UP STUDY.

Bozkurt OH, Aydemir H, Goker Z, et al.

OBJECTIVE: This study was aimed to evaluate medication profiles, adverse effects, and related factors in children with attention deficit hyperactivity disorder (ADHD).
METHODS: Clinical records of children who had diagnosis of ADHD and treated with medication between October 1st, and October 30th, 2015 were screened from the medical records of Department of Child Psychiatry at Ankara Pediatric Hematology Oncology Training and Research Hospital. From October 2015 to January 2016, follow up information (medication type, adverse effects, drop-out, changing in treatment) of these children was also recorded. Data obtained from this screening was analyzed with SPSS. Chi-square and Fisher's exact tests were used where appropriate. $p<0.05$ was accepted as significant.
RESULTS: Six hundred and seventeen of them with ADHD treated with medication in one month period were obtained from the hospital's medical records and included to this study. 77% of them were male and 23% of them were female. 28.7% of them were very first treated for ADHD. The median age of all subjects was 10. 79.4% of children were using psychostimulants and 20.6% of them were using non-stimulants. For the first time treated group (n=177), it was also found that stimulants were the first choice treatment of ADHD (79.1% of all). Drop-out ratio of first time treated children during 4 months follow up was 13% (n=23). Any adverse effect was detected in 10.7% (n=66) of all subjects and there was no statistically significant difference between genders (p=0.148). There was also no significant difference between taking stimulant or non-stimulant medications for developing adverse effects (p=0.830). The profile of adverse effects was the following: there were no side effects reported in 85.6% of all children, whereas 10.7% of them experienced an adverse effect (3.7%, n=23 missing data). 6% of them experienced any central nervous system side effects, 2.6% of all reported gastrointestinal system, 0.5% of them pointed a cardiovascular system, and 1.6% of all (n=10) experienced the other side effects. In 4.5% of all cases medication type was needed to be changed with another medication agent for ADHD treatment or a decrease in dosage of medication for dealing with the adverse effect they experienced. There was no statistical difference between using psychostimulant or non-stimulant in terms of changing or lowering dosage of medication (p=0.715). There was also no statistically significant difference between genders in terms of changing medication due to their adverse effects (p=0.475). Also no difference was found between the medication types regarding the changes in dosage or drugs itself one another (p=0.926).
CONCLUSIONS: Methylphenidate-derived psychostimulants are very first preferable drugs to treat ADHD. All medications were very-well tolerated in 85.67% of all subjects. 4.5% of treatments for all participants needed to be changed either in their dosage or in changing with another ADHD medication agent for adverse effects stemming from drugs

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Klin Psikofarmakol Bul. 2016;26:S16.

EFFECTS OF ATTENTION DEFICIT AND HYPERACTIVITY DISORDER ON CHILD MALTREATMENT.

Gokten ES, Duman NS, Soylu N, et al.

OBJECTIVE: Attention Deficit and Hyperactivity Disorder (ADHD) is a neurodevelopmental disorder that develops with inattention, hyperactivity, and impulsivity, which are not appropriate for age and level of development. In population-based studies questioning adult cases retrospectively in terms of ADHD symptoms and child abuse; the symptoms of childhood ADHD are associated with self-reported child abuse (Our study aimed at children diagnosed with ADHD who applied to the outpatient clinic of child and adolescent psychiatry unit for receiving the treatment. The aim of this study is to compare children diagnosed with ADHD with healthy children, and determine how all types of child abuse would vary between groups.
METHODS: The sample of the study consisted of children aged between 6-12 who presented to the outpatient clinic of Child and Adolescent Psychiatry Unit at Bursa Yuksek Ihtisas Training and Research Hospital between January and June 2015 and were diagnosed with ADHD by a child and adolescent psychiatrist according to the DSM-IV diagnostic criteria. The control group also included healthy children aged between 6-12 who presented to the outpatient clinic of Pediatric Surgery Unit at the same hospital with the pre-diagnoses of circumcision, inguinal hernia or acute appendicitis between the same dates and was

evaluated by a child and adolescent psychiatrist. In the both study groups, first the socio-demographic data form that was prepared by researchers were filled in by parents. Then, questions in the Abuse Evaluation Questionnaire were individually asked by a child and adolescent psychiatrist to children in a room without presence of parents.
RESULTS: A total 104 subjects from both ADHD and control groups (20.2% female (n=21), 79.8% male (n=83)) were included in the study. The average age was determined as 9.51±1.71 (min:6, max:12) in the ADHD group and 9.12±1.89 (min:6, max:12) in the control group. No statistically significant differences were found between the age and gender in study groups (p=0.122). When ADHD and control groups were compared, it was found that children with ADHD were exposed to a greater physical and emotional abuse and neglect was found at a higher rate in healthy control group, and there were no differences between the groups in terms of being exposed to sexual abuse and domestic violence. In the multiple logistic regression analysis when socioeconomic level, age and parental education were controlled; the independent factors related with ADHD were determined as behaviors like pulling hair, pulling ear or pinching, behaviors like slapping, punching or kicking, hitting with a belt, stick, ruler, wishing she/ he had never been born or threatening with leaving, mocking, insulting, giving a name, not meeting her/his needs despite having money, thinking that she/ he does not receive adequate care, and witnessing two adults brawling at home (p<0.05).
CONCLUSIONS: ADHD is a risk factor for physical and emotional abuse regardless of its sub-types and accompanying disruptive behavior disorders. While evaluating the cases, emphasizing this significant feature is important in terms of protection, follow-up, and treatment success

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Klin Psikofarmakol Bul. 2016;26:S70-S71.

CLINICAL CHARACTERISTICS AND TREATMENT RESPONSE IN PRESCHOOL ADHD: EXPERIENCE FROM A TERTIARY REFERRAL CENTER.

Ekinci O, Killi Y, Gunes S, et al.

OBJECTIVE: Although ADHD is typically first diagnosed in elementary school years, onset is commonly in preschool period. This retrospective chart review study examined the clinical characteristics and treatment response of preschool aged children with ADHD from a tertiary referral center.
METHODS: A total of 112 children, aged before 72 months of age, with documented DSM-IV ADHD diagnosis (including subtypes) were included. For a stable and valid ADHD diagnosis, only the patients who fulfilled DSM-IV diagnostic criteria on at least two separate clinical visits were included. The subjects with the diagnosis of intellectual disability, autism spectrum disorder and those who use of psychotropic medications other than study medications were excluded. Clinical and familial characteristics of the sample were obtained from the medical records and structured psychiatric interviews according to the DSM-IV (SCID-I). Treatments were grouped as follows: Behavioral treatment, Methylphenidate (MPH) and Risperidone. Improvement and side effects (at the 8th week) were assessed with Clinical Global Impression-Improvement (CGI-I) Scale and the adverse effect scale developed by the authors, respectively. For the secondary analysis of CGI-I, the scores of much improved and very much improved were collected and labeled as general improved. Treatment compliance was defined as the continuation of the selected treatment for at least 4 months on almost everyday.
RESULTS: The mean age of the sample was 56.9±12.7 months, 69% (n=78) were boys. The most frequent primary complaint was hyperactivity, followed by aggression and impulsivity. 75.8% of the sample had ADHD combined type diagnosis while the frequency of predominantly hyperactive-impulsive type was 18.8%. One-third of our sample had a comorbid DSM-IV diagnosis and the most frequent diagnoses were oppositional defiant disorder (ODD) (20.7%), anxiety disorder (10.7%), and conduct disorder (4%). At the 8th week, the frequency of general improvement was highest in the methylphenidate (MPH) group (80%), followed by behavioral (47%), and risperidone treatments (43%) (MPH vs. risperidone: p=0.023; MPH vs. behavioral treatment: p=0.018). Treatment compliance at the 16th week was 87% for risperidone, 76.1% for MPH and 36.3% for behavioral treatment. Both the risperidone (p=0.001) and MPH (p=0.002) treatments had a higher compliance than behavioral treatment. The frequency of any adverse effects was 38% and 26.8% in the MPH and risperidone groups, respectively (p=0.260). The frequency of severe adverse effects was very low in both groups (n=1). None of the study variables were found to be associated with the efficacy of MPH.

CONCLUSIONS: In this preliminary study on Turkish preschool children with ADHD, the clinical characteristics of our sample were found to be broadly similar to the previous studies' findings. MPH treatment was found to have a high level of efficacy and treatment compliance but a low level of tolerability. Stimulant treatment may be considered as an easy-to-use and effective treatment choice in preschool children with ADHD. However, because of the low tolerability, a close follow-up is a must. Psychosocial interventions, although being free of adverse effect risk, have moderate efficacy, and low treatment compliance. Certain psychosocial factors might be associated with the low efficacy of behavioral interventions

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Klin Psikofarmakol Bul. 2016;26:S42-S43.

SERUM ADRENOMEDULLIN AND NITRIC OXIDE LEVELS OF ATTENTION DEFICIT HYPERACTIVITY DISORDER DIAGNOSED PATIENTS AND THEIR ROLE IN ETIOPATHOGENESIS.

Isildar Y, Unlu G, Buber A, et al.

OBJECTIVE: Attention deficit hyperactivity disorder (ADHD) is a common childhood-onset neuropsychiatric disorder that affects the child's quality of life. Adrenomedullin (ADM) is a molecule that composed of 52 amino acids within the peptide structure. Nitric oxide (NO) is either a well known neurotransmitter of the central nervous system or one of the reactive oxygen species. ADM and NO have a regulatory role together in many organs and systems. Current data has showed that ADM and NO may have a role in the pathogenesis of certain psychiatric disorders such as schizophrenia, autism and affective disorders. In the present study, it is aimed to assess the role of ADM and NO in the etiopathogenesis of ADHD.
METHODS: Thirty patients between 6 and 16 years-old who have been firstly ADHD diagnosed and 30 healthy volunteer controls were included in the study. All participants were screened for psychiatric disorders by using the Schedule for Affective Disorders and Schizophrenia for School Aged Children, Present and Lifetime Version (K-SADS-PL). The Conner's Parent Rating Scale Short Version (CPRS- 48) was filled by parents in for the purpose of supporting the diagnosis. While Enzyme-Linked Immunosorbent Assay (ELISA) method was used for the measurement of ADM, and Spectrophotometer was used for the detection of NO in serum.
RESULTS: As a result of the study serum ADM and NO levels were found significantly lower in the ADHD group ($p<0.001$). No significant relationship was found between serum ADM and NO levels and CPRS-48 subscale scores for both of the groups ($p>0.05$); and a positive low correlation was found between serum ADM and NO levels in the patient group ($p<0.05$).
CONCLUSIONS: To the best of our knowledge, this is the first study that examines ADM levels in ADHD. Previous reports reveal that there are contradictory findings regarding the relationship between ADHD and NO. These results may indicate a more complex role of NO in ADHD. The etiology of ADHD is not well-known but the reduced activity of the dopaminergic and noradrenergic systems play a crucial role in ADHD pathogenesis. There is also evidence for glutamatergic dysregulation in ADHD. NO has effects on the release of dopamine, norepinephrine and glutamate. So low levels of NO are thought to be related to dopaminergic, noradrenergic and glutaminergic dysfunction in ADHD. Cerebral hypoperfusion and the hypothalamic-pituitary-adrenal (HPA) axis dysfunction in ADHD are reported by numerous studies. ADM and NO have a role in cerebral angiogenesis and perfusion and they have stimulating effect on HPA axis. Lower serum levels of ADM and NO may contribute to cerebral hypoperfusion and HPA axis dysfunction in ADHD. Both ADM and NO have also neuroprotective effects on central nervous system. Lower levels of ADM and NO may not provide adequate neuroprotection in ADHD patients. For a better understanding the role of ADM and NO in ADHD etiopathogenesis, further studies with a larger number of cases are needed

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Med Sci Monit. 2017;23:1378-84.

ASSOCIATION OF ATTENTION DEFICIT HYPERACTIVITY DISORDER AND AUTISM SPECTRUM DISORDERS WITH MEAN PLATELET VOLUME AND VITAMIN D.

Garipardic M, Do-ƒan M, Bala KA, et al.

Background: The purpose of this study was to assess the values of the mean platelet volume (MPV) in children with attention deficit hyperactivity disorder (ADHD) and with autism spectrum disorders (ASDs) to determine the risk of cardiovascular disease in these 2 disorder groups.

Material/Methods: The study included a total of 79 patients with ADHD or ASDs and controls in the Van region of Turkey. The control group included subjects of matching age and sex with no ADHD, ASDs, or chronic disease and taking no vitamins. The hematological parameters of the patients, including MPV, vitamin B12, and vitamin D, were assessed.

Results: The study included a total of 79 children and adolescents aged 2–18 years (32 females and 47 males). Of the patients, 36 were in the ADHD group, 18 in the ASDs group, and 25 in the control group. There was no statistically significant difference in hematological parameters between the groups, but there were significant differences in terms of vitamin D and vitamin B12. The patient groups showed lower levels of vitamin B12 and vitamin D. In the ADHD group, there was a negative correlation between both vitamins and MPV ($p<0.05$). Partial correlation analysis of the ADHD group showed that MPV in particular was negatively correlated to vitamin D, and not to vitamin B12 (p: 0.03).

Conclusions: Both ADHD and ASDs may accompany increased risk for cardiovascular disease due to the presence of vitamin B12 and D deficiency and their own characteristics. Therefore, these disorders should be closely followed up

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MMWR Morb Mortal Wkly Rep. 2017 Jan;65:1470-73.

ADVERSE HEALTH EFFECTS ASSOCIATED WITH LIVING IN A FORMER METHAMPHETAMINE DRUG LABORATORY - VICTORIA, AUSTRALIA, 2015.

Wright J, Kenneally ME, Edwards JW, et al.

The manufacture of methamphetamine in clandestine drug laboratories occurs in various locations, including residential houses and apartments. Unlike the controlled manufacture of chemicals and drugs, clandestine manufacture results in the uncontrolled storage, use, generation, and disposal of a wide range of chemicals and the deposit of methamphetamine drug residues on indoor surfaces (1). These residues have been found at high levels on porous and nonporous surfaces and have been shown to persist for months to years (1). Persons exposed to these environments often have poorly defined exposures and health effects. It is commonly assumed that these levels of exposure are low compared with those related to illicit drug use or therapeutic use of amphetamine-based drugs for managing behavioral issues such as attention deficit hyperactivity disorder (2). In 2015, a family that was unknowingly exposed to methamphetamine residues in a house in Australia was found to have adverse health effects and elevated methamphetamine levels in hair samples, highlighting the potential for public health risks for persons who might live in methamphetamine-contaminated dwellings. This case study highlights the importance of the identification and effective decontamination of former clandestine drug laboratories

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Movement Disorders Clinical Practice. 2017.

OUTPATIENT TREATMENT OF TIC DISORDERS AMONG CHILDREN AND ADULTS.

Smith JL, Gregory S, Mcbride N, et al.

Introduction: Limited information is available regarding treatment practices in applied settings for children and adults with tic disorders (TDs). We describe, for the first time, the treatment of TDs in U.S. children and adults in the outpatient setting.

Methods: Data from the 2003-2010 National Ambulatory Medical Care Survey and the National Hospital Ambulatory Care Survey were used. Descriptive statistics for modality of treatment and class of pharmacological medications were reported by patient and visit characteristics. Separate multivariable

logistic regression models were used to examine associations between patient and visit characteristics and classes of medications prescribed.
Results: One third (n = 99) of the sample did not receive any psychiatric or psychological treatment. Nearly two-thirds received a psychotropic medication. The most common class of medication was alpha-2 agonists (25%), followed by stimulants (23%), serotonin-reuptake inhibitors (SRIs) (19%), atypical antipsychotics (18%), anxiolytics (14%), anticonvulsants (11%), and typical antipsychotics (8%). Comorbid disorders and chronicity of problems were significantly associated with the receipt of certain classes of medications. Relatively few patients (18%) received psychotherapy.
Conclusions: If the decision is made to treat tic disorders, the choice of medication is dependent on the primary complaints, severity, chronicity, and the presence of comorbid psychiatric disorders. In general, comorbid externalizing, anxiety and mood disorders appear to influence treatment decisions in addition to TDs

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NASN Sch Nurse. 2016 May;31:153-57.
HOW THE SCHOOL NURSE CAN HELP IMPROVE THE EFFECTIVENESS OF ADHD MEDICATION.
Platt LM, Koch RL.

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NCHS Data Brief. 2017 Jan;1-8.
PHYSICIAN OFFICE VISITS FOR ATTENTION-DEFICIT/HYPERACTIVITY DISORDER IN CHILDREN AND ADOLESCENTS AGED 4-17 YEARS: UNITED STATES, 2012-2013.
Albert M, Rui P, Ashman JJ.
KEY FINDINGS: Data from the National Ambulatory Medical Care Survey *During 2012-2013, an estimated annual average of 6.1 million physician office visits were made by children aged 4-17 years with a primary diagnosis of attention-deficit/hyperactivity disorder (ADHD). *The ADHD visit rate among children aged 4-17 years was more than twice as high for boys (147 per 1,000 boys) as for girls (62 per 1,000 girls). *Central nervous system stimulant medications were provided, prescribed, or continued at about 80% of ADHD visits among children aged 4-17 years. *Among ADHD visits by children aged 4-17 years, 29% included a diagnostic code for an additional mental health disorder. *A total of 48% of visits for ADHD by children aged 4-17 years were with pediatricians, 36% were with psychiatrists, and 12% were with general and family practitioners. Attention-deficit/hyperactivity disorder (ADHD) is one of the most commonly diagnosed neurobehavioral disorders of childhood (1-3). ADHD is characterized clinically by inattention and/or hyperactivity-impulsivity that interferes with functioning or development (4). This report describes the rate and characteristics of physician office visits by children aged 4-17 years with a primary diagnosis of ADHD. Four years of age was chosen as the lower limit because the American Academy of Pediatrics guidelines for the diagnosis and treatment of ADHD begin at this age (5)

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Neurologia. 2017;32:158-65.
ATTENTION DEFICIT HYPERACTIVITY DISORDER: FROM PARENTS TO CHILDREN.
Vélez-van-Meerbeke A, et al.
Introduction Multiple studies of attention deficit hyperactivity disorder (ADHD) have recognised a heritability factor in that a higher frequency of the disorder is observed in children with an affected relative. Our aim was to determine the association between ADHD symptoms in young children enrolled in five schools in Bogota and a history of ADHD symptoms in their parents using the Wender-Utah Rating Scale.
Methodology Case-control study of participants selected according to DSM-IV criteria for ADHD and the Behavioral Assessment System for Children (BASC) completed by parents and teachers; the WISC-IV scale was used to exclude children with cognitive deficit. Parents completed the Wender-Utah Rating Scale to retrospectively identify any ADHD symptoms in childhood. A score of 36 was used as a cutoff point.

Results The study included 202 children: 117 cases and 85 controls. A positive history of ADHD symptoms in childhood was identified for 16% of 175 mothers and 20.6% of 141 fathers. The presence of symptoms in either parent, especially the mother, constitutes a significant risk factor for ADHD in children and this relationship persists after controlling for different variables. If both parents have the disorder, the risk tends to increase.
Conclusion Although ADHD has been linked to a genetic component, other environmental factors may be involved in the disorder

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Neuropsychiatr Dis Treat. 2017;13:667-83.

EFFECTS OF A STRUCTURED 20-SESSION SLOW-CORTICALPOTENTIAL-BASED NEUROFEEDBACK PROGRAM ON ATTENTIONAL PERFORMANCE IN CHILDREN AND ADOLESCENTS WITH ATTENTION-DEFICIT HYPERACTIVITY DISORDER: RETROSPECTIVE ANALYSIS OF AN OPEN-LABEL PILOT-APPROACH AND 6-MONTH FOLLOW-UP.

Albrecht JS, Bubenzer-Busch S, Gallien A, et al.

OBJECTIVE: The aim of this approach was to conduct a structured electroencephalography-based neurofeedback training program for children and adolescents with attention-deficit hyperactivity disorder (ADHD) using slow cortical potentials with an intensive first (almost daily sessions) and second phase of training (two sessions per week) and to assess aspects of attentional performance.
PATIENTS AND METHODS: A total of 24 young patients with ADHD participated in the 20-session training program. During phase I of training (2 weeks, 10 sessions), participants were trained on weekdays. During phase II, neurofeedback training occurred twice per week (5 weeks). The patients' inattention problems were measured at three assessment time points before (pre, T0) and after (post, T1) the training and at a 6-month follow-up (T2); the assessments included neuropsychological tests (Alertness and Divided Attention subtests of the Test for Attentional Performance; Sustained Attention Dots and Shifting Attentional Set subtests of the Amsterdam Neuropsychological Test) and questionnaire data (inattention subscales of the so-called Fremdbeurteilungsbogen für Hyperkinetische Störungen and Child Behavior Checklist/4-18 [CBCL/4-18]). All data were analyzed retrospectively.
RESULTS: The mean auditive reaction time in a Divided Attention task decreased significantly from T0 to T1 (medium effect), which was persistent over time and also found for a T0-T2 comparison (larger effects). In the Sustained Attention Dots task, the mean reaction time was reduced from T0-T1 and T1-T2 (small effects), whereas in the Shifting Attentional Set task, patients were able to increase the number of trials from T1-T2 and significantly diminished the number of errors (T1-T2 & T0-T2, large effects).
CONCLUSION: First positive but very small effects and preliminary results regarding different parameters of attentional performance were detected in young individuals with ADHD. The limitations of the obtained preliminary data are the rather small sample size, the lack of a control group/a placebo condition and the open-label approach because of the clinical setting and retrospective analysis. The value of the current approach lies in providing pilot data for future studies involving larger samples

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Neuropsychiatr Dis Treat. 2017;13:873-80.

DYNAMIC BALANCE IN CHILDREN WITH ATTENTION-DEFICIT HYPERACTIVITY DISORDER AND ITS RELATIONSHIP WITH COGNITIVE FUNCTIONS AND CEREBELLUM.

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

Background: Attention-deficit hyperactivity disorder (ADHD) is linked to the presence of motor deficiencies, including balance deficits. The cerebellum serves as an integrative structure for balance control and is also involved in cognition, including timing and anticipatory regulation. Cerebellar development may be delayed in children and adolescents with ADHD, and inconsistent reaction time is commonly seen in ADHD. We hypothesized that dynamic balance deficits would be present in children with ADHD and they would correlate with attention and cerebellar functions.
Methods: Sixty-two children with ADHD and no other neurological conditions and 62 typically developing (TD) children were examined with five trials of the Phyaction Balance Board, an electronic balancing platform.

Cerebellar clinical symptoms were evaluated using an international ataxia rating scale. ConnersΓÇÖ Continuous Performance Test was used to evaluate patterns of reaction.
Results: Children with ADHD had poorer performance on balancing tasks, compared to TD children (P,0.001). They exhibited significantly greater sway amplitudes than TD children (P,0.001) in all of the five balancing trials. The effect size of the difference between the groups increased continuously from the first to the last trial. Balance score in both groups was related to the variation in the reaction time, including reaction time standard error (r =0.25; P=0.0409, respectively, r =0.31; P=0.0131) and Variability of Standard Error (r =0.28; P=0.0252, respectively, r =0.41; P,0.001). The burden of cerebellar symptoms was strongly related to balance performance in both groups (r =0.50, P,0.001; r =0.49, P=0.001).
Conclusion: This study showed that ADHD may be associated with poor dynamic balance control. Furthermore, we showed that maintaining balance correlates with neuropsychological measures of consistency of reaction time. Balance deficits and impaired cognitive functioning could reflect a common cerebellar dysfunction in ADHD children

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Neuropsychiatr Dis Treat. 2017;13:785-92.
ATTENTION-DEFICIT HYPERACTIVITY DISORDER IN ELEMENTARY SCHOOL STUDENTS IN SHANTOU, CHINA: PREVALENCE, SUBTYPES, AND INFLUENCING FACTORS.
Huang Y, Zheng S, Xu C, et al.
Attention-deficit hyperactivity disorder (ADHD) is a frequent childhood-onset psychiatric condition and categorized into three subtypes of predominantly inattentive (ADHD-I), hyperactive impulsive (ADHD-H), and combined (ADHD-C). The prevalence and subtypes of ADHD vary considerably. The primary aim of this study was to provide a prevalence estimate of ADHD in elementary school students living in Shantou, a district of China, and in addition to examine the influence of informants, age, and gender on the prevalence. A total of 3,497 students aged 7–12 years were enrolled by random and stratified sampling. In stage I, teachers and parents of all participating students in randomly selected schools were asked to complete Chinese versions of the ConnersΓÇÖ 10-item scale. In stage II, students with high scores (>15) were interviewed by a psychiatrist for a diagnosis with or without ADHD. Parents rated many more students with high scores than teachers did in stage I. The prevalence of ADHD determined by Diagnostic and Statistical Manual of Mental Disorders, fifth edition (DSM-5) was 5.91% (5.27%–6.55%), which is comparable to the rates reported in previous studies with Chinese children. This hits the low border of the ADHD prevalence range from 5.9 to 7.1% worldwide, and is lower than that of Chinese children living in Hong Kong, suggesting an important influence of Chinese culture on the diagnosis of ADHD. The constituent ratios of ADHD-I, ADHD-C, and ADHD-H subtypes were 67.43, 24.57, and 8.00%, respectively. The rate of ADHD-H decreased with age, whereas that of ADHD-I remained at the highest levels in all age groups, suggesting that symptoms in the inattention domain are the most persistent and refractory

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Neuropsychology. 2017.
ATTENTION-DEFICIT/HYPERACTIVITY DISORDER AND PHONOLOGICAL WORKING MEMORY: METHODOLOGICAL VARIABILITY AFFECTS CLINICAL AND EXPERIMENTAL PERFORMANCE METRICS.
Tarle SJ, Alderson RM, Patros CHG, et al.
Objective: Despite promising findings in extant research that suggest impaired working memory (WM) serves as a central neurocognitive deficit or candidate endophenotype of attention-deficit/hyperactivity disorder (ADHD), findings from translational research have been relatively underwhelming. This study aimed to explicate previous equivocal findings by systematically examining the effect of methodological variability on WM performance estimates across experimental and clinical WM measures.
Method: Age-matched boys (ages 8-12 years) with (n = 20) and without (n = 20) ADHD completed 1 experimental (phonological) and 2 clinical (digit span, letter-number sequencing) WM measures.
Results: The use of partial scoring procedures, administration of greater trial numbers, and high central executive demands yielded moderate-to-large between-groups effect sizes. Moreover, the combination of

these best-case procedures, compared to worst-case procedures (i.e., absolute scoring, administration of few trials, use of discontinue rules, and low central executive demands), resulted in a 12.5% increase in correct group classification.
Conclusion: Collectively, these findings explain inconsistent ADHD-related WM deficits in previous reports, and highlight the need for revised clinical measures that utilize best-case procedures

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New Microbiol. 2016 Jul;39:237-39.
FIRST EVIDENCE OF HERV-H TRANSCRIPTIONAL ACTIVITY REDUCTION AFTER METHYLPHENIDATE TREATMENT IN A YOUNG BOY WITH ADHD.
D'Agati E, Pitzianti M, Balestrieri E, et al.
Human endogenous retroviruses (HERVs) have been associated with many complex diseases including neuropsychiatric diseases, such as attention deficit hyperactivity disorder (ADHD). In ADHD an over-expression of HERV-H family in peripheral blood mononuclear cells has been documented. It has been hypothesized that HERVs may represent the link between genetic and environmental risk factors, contributing to the clinical onset and/or to the progression of the neurodevelopmental disease. The effect of pharmacological treatment on HERV transcriptional activity in psychiatric disorders has been attracting attention. Using a real-time RT-PCR we investigated the influence of methylphenidate on HERV transcription in peripheral blood mononuclear cells of a young patient with ADHD. In this clinical case we describe for the first time the reduction of HERV-H expression and the significant improvement of ADHD symptoms after 6 months of methylphenidate treatment

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Nicotine Tob Res. 2017;19:94-101.
SECONDHAND SMOKE EXPOSURE AND LOW BLOOD LEAD LEVELS IN ASSOCIATION WITH ATTENTION-DEFICIT HYPERACTIVITY DISORDER AND ITS SYMPTOM DOMAIN IN CHILDREN: A COMMUNITY-BASED CASE-CONTROL STUDY.
Joo H, Lim MH, Ha M, et al .
Aim: Secondhand smoke (SHS) is a major indoor pollutant. We examined the possible association between exposure to both SHS and low levels of lead and attention-deficit-hyperactivity disorder (ADHD) and its symptom domain in children.
Methods: This case-control study was based on the results of a community survey using the ADHD rating scale conducted in 49 elementary schools. Both cases and control subjects were confirmed by a child psychiatrist. Each case was matched with one control subject according to gender, school, and grade in school. Using a multivariate conditional logistic regression model, we analyzed 214 case-control pairs of children who ranged in age from 6 to 10 years. Urine and blood levels of cotinine and of lead were determined, and information pertaining to SHS exposure was obtained by means of a questionnaire.
Results: Exposure to low levels of lead (geometric mean = 1.65 ++g/dL) was related to ADHD, particularly inattention (odds ratio [OR] = 1.67, 95% confidence interval [CI] = 1.07-2.59), whereas SHS exposure was associated mainly with hyperactivity/impulsivity (OR = 3.85, 95% CI = 1.55-9.56). In the pathway from blood lead to hyperactivity/impulsivity, children's SHS exposure mediated and indirectly accounted for about 73% of this relationship. The combined exposure to lead and SHS synergistically increased the risk of ADHD, evident as both inattention and hyperactivity/ impulsivity.
Conclusion: SHS, which is associated with hyperactivity/impulsivity in particular, combined with exposure to low blood levels of lead synergistically increased the risk of ADHD. Therefore, the exposure of children to both SHS and lead needs to be reduced

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Nutrients. 2016 Jun;8.

DIETARY, NUTRIENT PATTERNS AND BLOOD ESSENTIAL ELEMENTS IN CHINESE CHILDREN WITH ADHD.

Zhou F, Wu F, Zou S, et al.

Dietary or nutrient patterns represent the combined effects of foods or nutrients, and elucidate efficaciously the impact of diet on diseases. Because the pharmacotherapy on attention deficit hyperactivity disorder (ADHD) was reported be associated with certain side effects, and the etiology of ADHD is multifactorial, this study investigated the association of dietary and nutrient patterns with the risk of ADHD. We conducted a case-control study with 592 Chinese children including ADHD (n = 296) and non-ADHD (n = 296) aged 6-14 years old, matched by age and sex. Dietary and nutrient patterns were identified using factor analysis and a food frequency questionnaire. Blood essential elements levels were measured using atomic absorption spectrometry. A fish-white meat dietary pattern rich in shellfish, deep water fish, white meat, freshwater fish, organ meat and fungi and algae was inversely associated with ADHD (p = 0.006). Further analysis found that a mineral-protein nutrient pattern rich in zinc, protein, phosphorus, selenium, calcium and riboflavin was inversely associated with ADHD (p = 0.014). Additionally, the blood zinc was also negatively related to ADHD (p = 0.003). In conclusion, the fish-white meat dietary pattern and mineral-protein nutrient pattern may have beneficial effects on ADHD in Chinese children, and blood zinc may be helpful in distinguishing ADHD in Chinese children

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Pediatr Ann. 2016 Dec;45:e408-e411.

PEDIATRICIANS AS PSYCHIATRISTS.

Traisman ES.

The overall health of children and teenagers is dependent on their physical and psychological health. As pediatricians, it is important to enquire about the mental health of children and adolescents at the well-child visit. Screening for depression and attention-deficit/hyperactivity disorder is an important component of that visit. Understanding these disorders and the long-term effects on both the child and family as well as managing psychotherapeutic and pharmacological treatments are now becoming a critical part of pediatric care for children and adolescents

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Pediatr Ann. 2016 Oct;45:e342-e348.

MENTAL HEALTH ISSUES IN FOSTER CARE.

Lohr WD, Jones VF.

Children in foster care have exceptional needs due to their histories of abuse, neglect, and increased exposure to violence. The rates of psychiatric symptoms and disorders, such as attention-deficit/hyperactivity disorder, posttraumatic stress disorder, and reactive attachment disorder, are much higher in children in foster care; furthermore, the rate of these children receiving psychotropic medications is 3 times that of children who are not in foster care. Pediatricians, in their role of providing a medical home, play a central role in safeguarding the physical and mental health of these children. By taking a trauma-informed approach to understanding the unique needs and gaps in their health care, pediatricians can improve the mental health and maximize outcome for children in foster care

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Pediatr Int. 2016 Jun;58:476-81.

ANXIETY REDUCTION ON ATOMOXETINE AND METHYLPHENIDATE MEDICATION IN CHILDREN WITH ADHD.

Snircova E, Marcincakova-Husarova V, Hrtanek I, et al.

BACKGROUND: Atomoxetine and methylphenidate are widely used to treat attention-deficit-hyperactivity disorder (ADHD) with similar effectiveness after 8 weeks of treatment, when atomoxetine has reached its a full effect. Both drugs have also been shown to have an effect on comorbid anxiety. To the best of our knowledge, no study has compared their effect on the dynamics of anxiety symptom reduction. The aim of

this study was to compare the medication effect on core and comorbid anxiety symptom dynamics in children with ADHD.
METHODS: Sixty-nine patients participated in the study: 36 patients were taking atomoxetine and 33 patients, methylphenidate. Therapeutic effect on core symptoms of ADHD was measured on the ADHD-rating scale IV, and symptoms of anxiety were measured using the Conners Parent Rating Scale (CPRS). Symptoms were measured prior to and every 2 weeks during 8 weeks of treatment.
RESULTS: There was a significant decrease in CPRS anxiety subscale score in both medication groups. Anxiety subscale score was significantly lower in the atomoxetine group in the fourth week, and lasted through to 8 weeks of medication.
CONCLUSION: Both atomoxetine and methylphenidate reduced the symptoms of ADHD and anxiety. Atomoxetine was more effective in anxiety symptom reduction from the fourth week of treatment

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Pediatrics. 2017;139.
SMOKING IN PREGNANCY AND CHILD ADHD.
Gustavson K, Ystrom E, Stoltenberg C, et al.
BACKGROUND AND OBJECTIVE: There is a well-documented association between maternal smoking during pregnancy and offspring attention-deficit/hyperactivity disorder (ADHD). The degree to which this reflects causal intrauterine effects or is due to unmeasured confounding is not clear. We sought to compare the association between maternal smoking during pregnancy and offspring ADHD with the associations with paternal smoking, grandmother's smoking when pregnant with mother, and maternal smoking in previous pregnancies. Each of these exposures is expected to be influenced by much of the same confounding factors as maternal smoking during pregnancy, but cannot have direct intrauterine effects. A sibling control design was also used.
METHODS: The current study used data from the Norwegian Mother and Child Cohort Study (n > 100 000 children). Mothers and fathers reported on smoking during pregnancy, and mothers reported on smoking in previous pregnancies and their mother's smoking when pregnant with them. Mothers reported on child ADHD symptoms at 5 years of age. Information about child ADHD diagnosis was obtained from the Norwegian Patient Registry.
RESULTS: Maternal smoking during pregnancy was not more strongly associated with offspring ADHD diagnosis than was paternal smoking, grandmother's smoking when pregnant with mother, or maternal smoking in previous pregnancies. Sibling control analyses showed no association between maternal smoking in pregnancy and child ADHD symptoms among siblings discordant for maternal smoking.
CONCLUSIONS: These results suggest that the association between maternal smoking during pregnancy and offspring ADHD is not due to causal intrauterine effects, but reflects unmeasured confounding

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Pers Individ Dif. 2017 Mar;107:219-27.
CLONINGER'S PERSONALITY DIMENSIONS AND ADHD: A META-ANALYTIC REVIEW.
Gomez R, Van Doorn G, Watson S, et al.
A meta-analysis of up to 20 datasets is reported that examined the relationships between Cloninger's personality dimensions and Attention Deficit Hyperactivity Disorder (ADHD). Cloninger's model comprises four temperament (Novelty-Seeking, Harm-Avoidance, Reward Dependence, and Persistence) and three character (Self-Directedness, Cooperation, and Self-Transcendence) dimensions. Major findings were that all personality dimensions, except Self-Transcendence, were significantly associated with ADHD. These associations had different directions and magnitudes of relationship with ADHD. The associations were especially strong for Novelty-Seeking and Self-Directedness, being positive for Novelty-Seeking and negative for Self-Directedness. In addition, the association between ADHD and Persistence was moderated by age (stronger in children than adults) and source (stronger in clinical samples than community samples). Further, the association between harm avoidance and ADHD was moderated by age (strong and significant in adults, but not significant in children). Findings are discussed in relation to past work and the different

strengths of the associations found between Cloninger's personality dimensions and ADHD, developmental differences in these relationships, implications for theoretical models of ADHD, the influence of biological and environmental factors in the expression of ADHD, implications for treatment and diagnosis, and the underlying processes for the relationships between personality and ADHD

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Pharmacology. 2017;99:84-88.

EVALUATION OF THE POTENTIAL PHARMACOKINETIC INTERACTION BETWEEN ATOMOXETINE AND FLUVOXAMINE IN HEALTHY VOLUNTEERS.

Todor I, Popa A, Neag M, et al.

BACKGROUND/AIMS: Attention deficit hyperactivity disorder (ADHD) is frequently associated with other psychiatric pathologies. Therefore, the present study investigated a possible pharmacokinetic interaction between atomoxetine (ATX), a treatment option for ADHD, and an antidepressant, namely, fluvoxamine (FVX).

METHODS: Designed as an open-label, non-randomized clinical trial, the study included 2 periods. In period 1 (reference), each subject received ATX 25 mg (single-dose), whereas in period 2 (test), all subjects were given a combination of ATX 25 mg + FVX 100 mg, following a 6-day pretreatment regimen with the enzymatic inhibitor. Non-compartmental methods were employed to determine the pharmacokinetic parameters of ATX and its main active metabolite (glucuronidated form), 4-hydroxyatomoxetine-O-glucuronide.

RESULTS: The results revealed significant differences between the study periods for Cmax, AUC0-t and AUC0-infinity values corresponding to ATX and its metabolite. Small, but statistically significant increases in AUC values were reported for both parent drug (1,583.05 ± 1,040.29 vs. 2,111.55 ± 1,411.59 ng*h/ml) and 4-hydroxyatomoxetine-O-glucuronide (5,754.71 ± 1,235.5 vs. 6,293.17 ± 1,219.34 ng*h/ml) after combined treatment of ATX and the enzymatic inhibitor.

CONCLUSION: FVX had a modest effect on the pharmacokinetics of ATX and 4-hydroxyatomoxetine-O-glucuronide. The presence or absence of any clinical consequences associated with this pharmacokinetic drug-drug interaction needs to be established in future studies

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Pharmacopsychiatry. 2016 Nov;49:217-18.

EDITORIAL TO CHILD AND ADOLESCENCE PSYCHOPHARMACOLOGY.

Juckel G.

The editors of Pharmacopsychiatry have decided in 2016 to prepare special issues regularly in order provide our readers volumes of the journal with a thematic focus 1. The first such special issue is dedicated to the field of child and adolescent psychopharmacology. Many young patients are treated with psychotherapeutic, but also pharmacotherapeutic, methods worldwide. Most of our psychopharmacological agents are not approved by the federal institutions for persons under 18 years old. However, severe mental illnesses like schizophrenia, depression, anxiety, ADHD, and bipolar disorder frequently require pharmacological treatments in children and adolescents. We also see a wide range of rather unspecific emotional and behavioral disturbances up to excitation crises or suicidal acts in this young population, so that we see the necessity for standardized and valid psychopharmacological treatment regimens based on meta-analyses, randomized controlled trials, and guidelines 2. Child and adolescent psychiatry is unfortunately far away from this; industry-supported research is rare in this area, but also not all child and adolescent psychiatrists see the importance of psychopharmacological treatment and trust specific psychotherapy, psychoeducation, and educational strategies. These are all extremely important treatments, but one can/should think that psychopharmacotherapy is an important addition and often a cornerstone for the other treatments

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PLoS ONE. 2016;11:e0154296.

NO EVIDENCE FOR DISEASE HISTORY AS A RISK FACTOR FOR NARCOLEPSY AFTER A(H1N1)PDM09 VACCINATION.

Lamb F, Ploner A, Fink K, et al.

OBJECTIVES: To investigate disease history before A(H1N1)pdm09 vaccination as a risk factor for narcolepsy.

METHODS: Case-control study in Sweden. Cases included persons referred for a Multiple Sleep Latency Test between 2009 and 2010, identified through diagnostic sleep centres and confirmed through independent review of medical charts. Controls, selected from the total population register, were matched to cases on age, gender, MSLT-referral date and county of residence. Disease history (prescriptions and diagnoses) and vaccination history was collected through telephone interviews and population-based healthcare registers. Conditional logistic regression was used to investigate disease history before A(H1N1)pdm09 vaccination as a risk-factor for narcolepsy.

RESULTS: In total, 72 narcolepsy cases and 251 controls were included (range 3-69 years mean19-years). Risk of narcolepsy was increased in individuals with a disease history of nervous system disorders (OR range = 3.6-8.8) and mental and behavioural disorders (OR = 3.8, 95% CI 1.6-8.8) before referral. In a second analysis of vaccinated individuals only, nearly all initial associations were no longer statistically significant and effect sizes were smaller (OR range = 1.3-2.6). A significant effect for antibiotics (OR = 0.4, 95% CI 0.2-0.8) and a marginally significant effect for nervous system disorders was observed. In a third case-only analysis, comparing cases referred before vaccination to those referred after; prescriptions for nervous system disorders (OR = 26.0 95% CI 4.0-170.2) and ADHD (OR = 35.3 95% CI 3.4-369.9) were statistically significant during the vaccination period, suggesting initial associations were due to confounding by indication.

CONCLUSION: The findings of this study do not support disease history before A(H1N1) pdm09 vaccination as a risk factor for narcolepsy

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PLoS ONE. 2017;12.

AN EVENT RELATED POTENTIAL STUDY OF IHIBITORY AND ATTENTIONAL CONTROL IN WILLIAMS SYNDROME ADULTS .

Greer JMH, Hamilton C, McMullon MEG, et al.

The primary aim of the current study was to employ event-related potentials (ERPs) methodology to disentangle the mechanisms related to inhibitory control in older adults with Williams syndrome (WS). Eleven older adults with WS (mean age 42), 16 typically developing adults (mean age 42) and 13 typically developing children (mean age 12) participated in the study. ERPs were recorded during a three-stimulus visual oddball task, during which participants were required to make a response to a rare target stimulus embedded in a train of frequent non-target stimuli. A task-irrelevant infrequent stimulus was also present at randomised intervals during the session. The P3a latency data response related to task-irrelevant stimulus processing was delayed in WS. In addition, the early perceptual N2 amplitude was attenuated. These data are indicative of compromised early monitoring of perceptual input, accompanied by appropriate orientation of responses to task-irrelevant stimuli. However, the P3a delay suggests inefficient evaluation of the task-irrelevant stimuli. These data are discussed in terms of deficits in the disengagement of attentional processes, and the regulation of monitoring processes required for successful inhibition

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Prim Care Companion CNS Disord. 2016 Dec;18.

DULOXETINE ALLEVIATES STIMULANT DYSPHORIA, HELPS WITH ENURESIS, AND COMPLEMENTS COGNITIVE RESPONSE IN AN ADOLESCENT WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.

Naguy A.

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Prim Care Companion CNS Disord. 2016;18.

FACTORS ASSOCIATED WITH MUSCULOSKELETAL INJURIES IN CHILDREN AND ADOLESCENTS WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.

Guy JA, Knight LM, Wang Y, et al.

BACKGROUND: Musculoskeletal injuries may be associated with attention-deficit/hyperactivity disorder (ADHD) symptom severity, comorbid psychiatric or medical conditions, and the prescribed psychostimulant.
METHODS: A population-based, retrospective cohort design was employed using South Carolina's Medicaid claims data set covering outpatient and inpatient medical services and medication prescriptions over an 11-year period (January 1, 1996, through December 31, 2006) for patients ≤ 17 years of age with ≥ 2 visits for ICD-9-CM diagnostic codes for ADHD. A cohort of 7,725 cases was identified and analyzed using logistic regression to compare risk factors for those who sustained focal musculoskeletal injuries and those who did not.
RESULTS: The risk of sustaining sprains, arthropathy and connective tissue disorders, or muscle and joint disorders was significantly related to being diagnosed with comorbid hypertension (adjusted odds ratios [aORs] = 1.60, 2.09, and 1.46, respectively) and a substance use disorder (aORs = 1.58, 1.38, and 1.28). Having a substance use disorder was also related to incident fractures and dorso/spinal injuries (aORs = 1.42 and 1.21). Diagnosed hypertension was related to incident concussions (aOR = 2.00), a diagnosed thyroid disorder was related to an increased risk of sprain and concussion (aORs = 1.44 and 2.05), a diagnosed anxiety disorder was related to an increased risk of dorso/spinal disorders (aOR = 1.71), and diagnosed diabetes was related to incident bone and cartilage disorders (aOR = 1.61).
CONCLUSIONS: Comorbid hypertension, substance use disorders, and thyroid disorders deserve increased clinical surveillance in children and adolescents with ADHD because they may be associated with an increased risk of more than one musculoskeletal injury

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Psychiatr Invest. 2017;14:158-65.

FACTORS THAT AFFECT THE ADHERENCE TO ADHD MEDICATIONS DURING A TREATMENT CONTINUATION PERIOD IN CHILDREN AND ADOLESCENTS: A NATIONWIDE RETROSPECTIVE COHORT STUDY USING KOREAN HEALTH INSURANCE DATA FROM 2007 TO 2011.

Bhang SY, Kwack YS, Joung YS, et al.

Objective Several factors, such as male gender, older age, type of insurance, comorbid conditions, and medication type, have been associated with attention-deficit/hyperactivity disorder (ADHD) medication adherence rates, but the results have been inconsistent. We analyzed data to answer several questions: 1) How old were patients who first refilled their treatment medications used primarily for ADHD, regardless of the medication type? 2) What socio-demographic factors are associated with medication adherence? 3) What medical conditions, such as medication type and comorbid diagnosis, influence adherence?
Methods We analyzed National Health Insurance data, which comprised continuously enrolled Korean National Medical Insurance children (6–18 years) with at least 2 ADHD prescription claims (January 2008–December 2011). The persistence of use regarding the days of continuous therapy without a 30-day gap were measured continuously and dichotomously. Adherence, using a medication possession ratio (MPR), was measured dichotomously (80% cut-off).
Results The cumulative incidence of index cases that initiated medication refills for ADHD treatment during the 4 year period was 0.85%. The patients who exhibited a MPR greater than 80 comprised approximately 66%. The medication type, high school age groups, physician speciality, treatment at a private clinic, and comorbid conditions were associated with medication adherence during continuous treatment using a multivariate analysis.
Conclusion A better understanding of ADHD treatment patterns may lead to initiatives targeted at the improvement of treatment adherence and persistence. Other factors, including the severity, family history, costs, type of comorbidities, and switching patterns, will be analyzed in future studies

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Psychiatry Res Neuroimaging. 2017;263:1-7.

A FUNCTIONAL CONNECTIVITY COMPARISON BETWEEN ATTENTION DEFICIT HYPERACTIVITY DISORDER AND BIPOLAR DISORDER IN MEDICATION-NA+»VE ADOLESCENTS WITH MOOD FLUCTUATION AND ATTENTION PROBLEMS.

Son YD, Han DH, Kim SM, et al.

In order to compare patterns of connectivity between affective and attention networks in adolescents with bipolar disorder (BD) and attention deficit hyperactivity disorder (ADHD), we investigated differences in resting state functional connectivity (RSFC) between these populations. Study participants were medication-na+»ve adolescents (aged 13–18 years) with BD (N=22) or ADHD (N=25) and age- and sex-matched healthy adolescents (healthy controls [HC]) (N=22). Forty-seven adolescents with mood fluctuation and attention problems showed increased functional correlation (FC) between two pairs of regions within the affective network (AFN), compared to 22 HC: the left orbitofrontal cortex (OFC) to the left thalamus and the left OFC to the right thalamus. In post-hoc testing, adolescents with BD showed increased FC between two pairs of regions compared to ADHD: the right amygdala to the left temporoparietal junction (TPJ) and the right amygdala to the right TPJ. Adolescents with BD showed increased FC within the attention network (ATN) as well as increased FC between the ATN and the AFN, while those with ADHD showed decreased FC within the ATN. The current suggests that these features could be used as biomarkers for differentiating BD from ADHD in adolescents

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Res Dev Disabil. 2016 Sep;56:18-28.

THE EFFECT OF PARENT EDUCATION PROGRAM FOR PRESCHOOL CHILDREN WITH DEVELOPMENTAL DISABILITIES: A RANDOMIZED CONTROLLED TRIAL.

Leung C, Chan S, Lam T, et al.

AIM: This study aimed to evaluate the efficacy of a parent education program, the Happy Parenting program, for Chinese preschool children with developmental disabilities.

METHODS: This study adopted randomized controlled trial design without blinding. Participants were randomized into intervention group (n=62) who were offered the Happy Parenting program delivered by educational psychologists and trainee educational psychologists, and a control group (n=57) who were offered a parent talk after the intervention group had completed treatment. Parent participants were requested to complete questionnaires on their children's behavior, their parenting stress, and discipline strategies.

RESULTS: Analysis was by intention-to-treat. The results indicated significant decrease in child problem behaviors, parenting stress and dysfunctional discipline strategies in the intervention group at post-intervention.

CONCLUSION: This study provided promising evidence on the effectiveness of a parent education program, the Happy Parenting program, for Chinese preschool children with developmental disabilities

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Res Dev Disabil. 2016 Dec;59:351-58.

HYPERFOCUSING AS A DIMENSION OF ADULT ATTENTION DEFICIT HYPERACTIVITY DISORDER.

Ozel-Kizil ET, Kokurcan A, Aksoy UM, et al.

Patients with Attention Deficit Hyperactivity Disorder (ADHD) suffer not only from inability to focus but also from inability to shift attention for events that trigger their interests. This phenomenon is called "hyperfocusing". Previous literature about hyperfocusing is scarce and relies mainly on case reports. The study aimed to investigate and compare the severity of hyperfocusing in adult ADHD with and without psycho-stimulant use. ADHD (DSM-IV-TR) patients either psycho-stimulant naive (n=53) or on psycho-stimulants (n=79) from two ADHD clinics were recruited. The control group (n=65) consisted of healthy university students. A socio-demographic form, the Beck Depression Inventory, the Wender-Utah Rating Scale, the Adult ADHD Self- Report Scale and the Hyperfocusing Scale were applied to the participants. There was no difference between total Hyperfocusing Scale and Adult ADHD Self- Report Scale scores of two patient groups, but both have higher scores than controls ($p<0.001$). Hyperfocusing is higher in adult ADHD and

there was no difference between stimulant-naive patients or patients on stimulants. Hyperfocusing can be defined as a separate dimension of adult ADHD

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Res Dev Disabil. 2016 Oct;57:18-28.

A CROSS-SYNDROME EVALUATION OF A NEW ATTENTION RATING SCALE: THE SCALE OF ATTENTION IN INTELLECTUAL DISABILITY.

Freeman NC, Gray KM, Taffe JR, et al.

Whilst neuropsychological research has enhanced our understanding of inattentive and hyperactive behaviours among children with intellectual disability (ID), the absence of rating scales developed for this group continues to be a gap in knowledge. This study examined these behaviours in 176 children with autism spectrum disorder (ASD), Down Syndrome (DS), or idiopathic ID using a newly developed teacher rating scale, the Scale of Attention in Intellectual Disability. Findings suggested that children with ASD had a significantly greater breadth of hyperactive/impulsive behaviours than those with DS or idiopathic ID. These findings support existing research suggesting differing profiles of attention and activity across groups. Understanding disorder-specific profiles has implications for developing strategies to support students with ID in the classroom

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Res Soc Work Pract. 2017 Jan;27:36-47.

EFFICACY OF PARENT CHILD INTERACTION THERAPY WITH CHINESE ADHD CHILDREN: RANDOMIZED CONTROLLED TRIAL.

Leung C, Tsang S, Ng GSH, et al.

Purpose: This study aimed to evaluate the efficacy of Parent-Child Interaction Therapy (PCIT) in Chinese children with attention-deficit/hyperactivity disorder (ADHD) or ADHD features.

Methods: This study adopted a randomized controlled trial design without blinding. Participants were randomized into either the intervention group (n = 32) and offered PCIT by trained PCIT practitioners or the waitlist control group (n = 32) and offered PCIT after the intervention group had completed treatment. Parent participants were requested to complete questionnaires on their children's behavior and their parental stress. PCIT practitioners observed parent–child interactions according to a coding system.

Results: Analysis was by intention to treat. The results indicated a significant decrease in child behavior and attention problems, parental stress, and negative parenting practices and an increase in positive parenting practices in the intervention group at postintervention ($p \leq .002$ in all cases).

Conclusion: This study provided promising evidence on the effectiveness of PCIT in Chinese children with ADHD or ADHD features

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Rev Colomb Psiquiatr. 2016 Dec;45 Suppl 1:39-49.

PREVALENCE AND ASSOCIATED FACTORS OF MENTAL DISORDERS IN COLOMBIAN CHILD POPULATION, THE 2015 NATIONAL MENTAL HEALTH SURVEY.

Gomez-Restrepo C, Auli J, Tamayo MN, et al.

INTRODUCTION: The 2015 National Mental Health Survey aimed to expand our knowledge about the real mental state of children in Colombia, taking into account the fact that most mental disorders in adults begin during childhood or adolescence. It is essential to have an improved knowledge of the magnitude of this issue and to design timely interventions that reduce long term complications.

OBJECTIVE: The aim of the study was to determine the prevalence of the disorders in the last 12 months and 30 days according to the DSM-IV, as well as to collect data about social and demographic variables.

METHODS: The structured Diagnostic Interview Schedule for Children (DISC-P), which provides DSM-IV diagnoses, was applied to carers of non-institutionalised children between 7 and 11 years old. The disorders evaluated included: major depressive disorder, dysthymia, generalised anxiety disorder, separation anxiety

disorder, attention deficit hyperactivity disorder in its three kinds (mixed, inattentive, and hyperactive), oppositional defiant disorder, and conduct disorder. The instrumentation was computer-assisted.
RESULTS: Prevalences of the disorders are present both in the last 30 days and in the last 12 months. In general, there is a prevalence of any of the disorders of 3% (95% CI, 2.2-4.0) in the last 30 days, and 4.7% (95% CI, 3.6-6.2) in the last 12 months. When evaluated individually, attention deficit hyperactivity disorder is the most frequent disorder, with a prevalence of 2.3% and 3.0% in the last 30 days and the last 12 months, respectively. In addition, the disorders that are known to frequently begin during childhood are the most common disorders in the age group studied, with a prevalence of 2.5% in the last 30 days and 3.2% in the last year.
CONCLUSIONS: The 2015 National Mental Health Survey provides precise information about the real mental situation in children between the ages of 7 and 11 years in Colombia, compared with past epidemiological studies in the country, which were restricted to specific populations. By improving the reliability on knowledge about mental disorders in children, it will be possible to design more appropriate and precise strategies for prevention, diagnosis, and treatment

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Sleep Med Clin. 2017 Mar;12:23-30.
SOCIOECONOMIC IMPACT OF PEDIATRIC SLEEP DISORDERS.
Yuen KM, Pelayo R.
Pediatric disorders tend to affect the immediate support unit, adults and children. High costs for direct consumption of medical care are offset by early diagnosis and treatment of pediatric sleep disorders. Pediatric sleep disorders are underdiagnosed and undertreated. Attention-deficit/hyperactivity disorder may result from insufficient or fragmented sleep. Delaying school start time resulted in decreased car crashes in teen drivers and improved mood

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Therapeutic Advances in Drug Safety. 2017;8:87-99.
ATTENTION-DEFICIT HYPERACTIVITY DISORDER MEDICATION USE: FACTORS INVOLVED IN PRESCRIBING, SAFETY ASPECTS AND OUTCOMES.
Martinez-Raga J, Ferreros A, Knecht C, et al.
While treatment of patients with attention-deficit hyperactivity disorder (ADHD) is based on a multimodal approach that combines medication with specific psychological interventions, pharmacotherapy alone is generally considered an essential and cost-effective element. This paper aims to comprehensively and critically review factors involved in prescribing and medication use in individuals diagnosed with ADHD, focusing on the difficulties facing patients with ADHD seeking treatment, as well as the safety and tolerability aspects of ADHD pharmacotherapies, with particular attention on the cardiovascular adverse events and the potential risk of misuse or diversion of ADHD medications. A comprehensive and systematic literature search of PubMed/MEDLINE database was conducted to identify studies published in peer-reviewed journals until 1 August 2016. Children, adolescents and adults often encounter significant difficulties in the process of accessing specialist assessment and treatment for ADHD as a consequence of disparities in service organization and available treatment provision. Despite the well-established efficacy and overall safety profile, ADHD medications are not exempt from adverse events. The cardiovascular safety of pharmacotherapies used for treating individuals with ADHD has raised particular concerns; however there is little evidence of serious cardiovascular adverse events, including no serious corrected QT (QTc) abnormalities associated with stimulants, atomoxetine or +¦2-adrenergic receptor agonists. Although the abuse of prescription stimulant drugs, particularly, short-acting stimulants is a prevalent and growing problem, nonmedical use of prescription stimulants within the clinical context is very limited. In addition, nonstimulant ADHD medications lack any reinforcing effects and consequently any abuse potential

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Therapeutics, Pharmacology and Clinical Toxicology. 2014;18:61-67.

ASSESSING THE EFFECTIVENESS AND SAFETY OF PHARMACOLOGICAL THERAPY IN CHILDREN DIAGNOSED WITH ATTENTION DEFICIT AND HYPERACTIVITY DISORDERS.

Maria DA, Elena T, Cristina N, et al .

Deficit Hyperactivity Disorder (ADHD) is considered to be a neurodevelopment condition with a worldwide prevalence between 3-10 % in children1 with symptoms that could continue into adolescence for 50-80% of cases and into adulthood for as many as 30 - 50 % of cases. The purpose of the research was to evaluate the efficacy and safety of pharmacological treatment in attention deficit hyperactivity children. A retrospective clinical research in 73 patients was designed and carried out at "Victor Gomoiu" Clinical Pediatric Hospital. The data was obtained from patients medical records. The study duration was 15 months from Jan 2013 to March 2014. The medical treatment was analysed: type of drugs given, dosage, pharmaceutical formulation, length of treatment. We also analysed the types of non-medical treatments associated: psychological therapy, logopedic therapy, occupational and cognitive stimulation therapy, other types of therapy. Monthly monitoring and identification of adverse events was done for each patient by analysing the type of medication given, adverse event onset, severity, dose optimization, withdrawal from treatment or change of medication. Data was stratified for three age groups: preschool children (< 7years old), 12 to 18 - year-olds and 7 to 11 - year- olds. Combined therapy (both medical and psychological) gave results but without being able to determine the measure in which either the psychological, pharmacological or combined treatment have influenced the end result. Early detection and management of side effects (dose optimization, change of medication, drug combinations that diminish or even eliminate the side effects, treatment interruption) improve compliance and adherence towards the given medical treatment but also improve the quality of life

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Trends Psychiatry Psychother. 2016 Apr;38:100-04.

PHONEMIC VERBAL FLUENCY AND SEVERITY OF ANXIETY DISORDERS IN YOUNG CHILDREN.

Toazza R, Salum GA, Jarros RB, et al .

INTRODUCTION: Previous studies have implicated impaired verbal fluency as being associated with anxiety disorders in adolescents.

OBJECTIVES: To replicate and extend previously reported evidence by investigating whether performance in phonemic verbal fluency tasks is related to severity of anxiety symptoms in young children with anxiety disorders. We also aim to investigate whether putative associations are independent from co-occurring attention deficit hyperactivity disorder (ADHD) symptoms.

METHODS: Sixty children (6-12 years old) with primary diagnoses of anxiety disorders participated in this study. Severity of symptoms was measured using clinician-based, parent-rated and self-rated validated scales. Verbal fluency was assessed using a simple task that measures the number of words evoked in 1-minute with the letter F, from which we quantified the number of isolated words, number of clusters (groups of similar words) and number of switches (transitions between clusters and/or between isolated words).

RESULTS: There was a significant association between the number of clusters and anxiety scores. Further analysis revealed associations were independent from co-occurring ADHD symptoms.

CONCLUSION: We replicate and extend previous findings showing that verbal fluency is consistently associated with severity in anxiety disorders in children. Further studies should explore the potential effect of cognitive training on symptoms of anxiety disorders

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Turk Psikiyatri Derg. 2016;27:31-40.

AALYZING THE WECHSLER INTELLIGENCE SCALE FOR CHILDREN-REVISED (WISC-R) IN CHILDREN WITH ATTENTION DEFICIT AND HYPERACTIVITY DISORDER: PREDICTIVE VALUE OF SUBTESTS, KAUFMAN, AND BANNATYNE CATEGORIES.

Tural HS, Celik C, Ozmen S, et al.

OBJECTIVE: The aim of this study is to evaluate the predictive value of intelligence quotients scores (IQs), subtests of Wechsler Intelligence Scale for Children-Revised (WISC-R) and Kaufman's and Bannatyne's

categories scores which are the sums of subtests of WISC-R in attention deficit hyperactivity disorder (ADHD). Another aim is to examine the difference of some neurocognitive skills between the children with ADHD and their unaffected peers by WISC-R subtests.
METHOD: WISC-R's subtest and IQ scores, and scores of Kaufman's and Bannatyne's categories of the children who were diagnosed with only ADHD were compared with the same scores of the children who were in healthy control group (N= 111) and were in ADHD with co morbidity group (N= 82).
RESULTS: It was found that the subtest scores (vocabulary, comprehension, digit span, picture completion and block design) of the children with only ADHD and ADHD with comorbidity were significantly lower than healthy group. It was observed that subtests of comprehension (Wald= 5.47, df= 1, p=0.05), digit span (Wald= 16.79, df= 1, p=0.001) and picture completion (Wald= 5.25, df= 1, p=0.05) predicted significantly ADHD. In addition, the categories of freedom from distractibility (Wald= 8.22, df= 1, p=0.01) and spatial abilities (Wald= 12.22, df= 1, p<0.0001) were predictive for ADHD in this study.
CONCLUSION: Problem solving abilities in social processes, auditory short-term memories, visual-spatial abilities and visual configuration abilities of the children with ADHD was observed to be lower than their healthy peers. It was thought that in WISC-R's profile analysis, the categories of freedom from distractibility and spatial abilities can be distinctive in ADHD diagnose

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Urol J. 2017 Jan;14:2968-72.
COMORBID PSYCHIATRIC DISORDERS IN CHILDREN AND ADOLESCENTS WITH NOCTURNAL ENURESIS.
Amiri S, Shafiee-Kandjani AR, Naghinezhad R, et al.
PURPOSE: The present study was conducted with the aim of identifying the frequency of comorbid psychiatricdisorders in children and adolescents with nocturnal enuresis (NE). MATERIALS AND
METHODS: In this descriptive-analytical study, 183 children and adolescents aged 5-18 years withNE referred to psychiatric clinics at Tabriz University of Medical Sciences were selected in 2015. A structuredclinical diagnostic interview, the kiddie-schedule for affective disorders and schizophrenia (K-SADS), was employedbased on the diagnostic and statistical manual of mental disorders (DSM-IV-TR) for the diagnosis of NEand comorbid psychiatric disorders.
RESULTS: In this study, 39 participants (21.3%) were female and 144 (78.7%) were male. The mean age of participantswas 8.69 ± 2.34 years. The lifelong incidence of mental disorders among enuretic children and adolescentswas 79.23%. The highest incidence belonged to attention deficit/hyperactivity disorder (ADHD) with 74.9%, oppositional-defiant disorder (ODD) with 53%, and tic disorders with 12% (motor tics together with a single caseof vocal tic). The lowest incidence was for conduct disorder, bipolar affective disorder, and post-traumatic stressdisorder (PTSD) with 5%. Based on the Fisher exact test, there was no significant difference between girls andboys in terms of psychiatric disorders incidence (P > .05).
CONCLUSION: Comorbid psychiatric disorders with NE are common among children and adolescents. Therefore,in-depth examination of other psychiatric disorders needs to be carried out in enuretic children and adolescents,which will affect the treatment and prognosis of NE

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World J Biol Psychiatry. 2017;1-21.
COMMON AND SPECIFIC GENES AND PERIPHERAL BIOMARKERS IN CHILDREN AND ADULTS WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.
Bonvicini C, Faraone SV, Scassellati C.
OBJECTIVES: Elucidating the biological mechanisms involved in Attention-deficit/hyperactivity disorder (ADHD) has been challenging. Relatively unexplored is the fact that these mechanisms can differ with age.
METHODS: We present an overview on the major differences between children and adults with ADHD, describing several studies from genomics to metabolomics performed in ADHD children and in adults. A systematic search (up until February, 2016) was conducted.
RESULTS: From a PRISMA flow-chart, a total of eligibility 350 studies from genomics and metabolomics were found for cADHD and 91 for aADHD. For children, associations were found for genes belonging to

dopaminergic (SLC6A3, DRD4, MAOA) and neurodevelopmental (LPHN3, DIRAS2) systems and OPRM1 (Yates Corrected p = 0.016; OR = 2.27 95%CI:1.15-4.47). Studies of adults have implicated circadian rhythms genes, HTR2A, MAOB and a more generic neurodevelopmental/neurite outgrowth network (BCHE, SNAP25, BAIAP2, NOS1/NO, KCNIP4, SPOCK3; Yates Corrected p = 0.007; OR= 3.30 95%CI:1.33-8.29). In common among cADHD and aADHD, the most significant findings are for oxidative stress proteins (MAD, SOD, PON1, ARES, TOS, TAS, OSI), and, in the second level, DISC1, DBH, DDC, microRNA and adiponectin.

CONCLUSIONS: Through a convergent functional genomics, this review contributes to clarify which genetic/biological mechanisms differ with age. The effects of some genes do not change throughout lifetime, whereas others are linked to age specific stages. Additional research and further studies are needed to generate firmer conclusions that might someday be useful for predicting the remission and persistence of the disorder. Although the limitations, some of these genes/proteins could be potential useful biomarkers to discriminate cADHD versus aADHD

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ANXIETY MODULATES THE RELATION BETWEEN ATTENTION-DEFICIT/HYPERACTIVITY DISORDER SEVERITY AND WORKING MEMORY-RELATED BRAIN ACTIVITY.

Van Der Meer D, Hoekstra PJ, van Rooij D, et al.

Objectives: Individuals with attention-deficit/hyperactivity disorder (ADHD) often have heightened levels of anxiety, which has been associated with worse performance on working memory tasks. Knowledge of the neural pathways underlying the combined presence of ADHD and anxiety may aid in a better understanding of their co-occurrence. Therefore, we investigated how anxiety modulates the effect of ADHD severity on neural activity during a visuospatial working memory (VSWM) task.

Methods: Neuroimaging data were available for 371 adolescents and young adults participating in the multicentre cohort study NeuroIMAGE (average age 17.1 years). We analysed the effects of ADHD severity, anxiety severity and their interaction on-task accuracy, and on neural activity associated with working memory (VSWM trials minus baseline), and memory load (high memory load trials minus low load trials).

Results: Anxiety significantly modulated the relation between ADHD severity and neural activity in the cerebellum for the working memory contrast, and bilaterally in the striatum and thalamus for the memory load contrast.

Conclusions: We found that ADHD with co-occurring anxiety is associated with lowered neural activity during a VSWM task in regions important for information gating. This fits well with previous theorising on ADHD with co-occurring anxiety, and illustrates the neurobiological heterogeneity of ADHD

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ADHD-LIKE SYMPTOMS IN CHILDREN AFFECTED BY OBSTRUCTIVE SLEEP APNEA SYNDROME: A CASE-CONTROL STUDY

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ABSTRACT

***Introduction**: ADHD is characterized by inattention, hyperactivity, impulsivity, or a combination of these symptoms. Sleep disorders may be considered as a not secondary underlying cause of ADHD and growing evidence evidenced that obstructive sleep apnea syndrome (OSA) symptoms may overlap ADHD's ones.*

Aim of the present study is verifying the presence of ADHD-like symptoms in other frequent condition such as sleep-related breathing disorders in pediatric age.

***Materials and methods**: 34 children (19 males and 15 females) aged 6-10 years (mean age 9.706 ± 3.434) with polysomnographic diagnosis of OSA, according to ICSD-3 criteria, were recruited. Control group was composed by 89 typical developing children (47 males, 42 females) (mean age 9,528 ± 3,351). The Conners' Rating Scale– Revised (CRS-R) test was administered to mothers to assess their children's behavior.*

***Results:** The two groups are comparable for age (p = 0.794) and sex distribution (p = 0.918). Subjects affected by OSA present higher scores in pathological range in all scales of CRS-R than controls (Table 1).*

***Conclusions**: Scientific and clinical evidences tend to stress the similarities between ADHD and OSA effects/comorbidities in pediatric age, suggesting sleep screening as mandatory before starting stimulant drugs treatment.*

***Keywords**: ADHD, ADHD-like symptoms, obstructive sleep apnea syndrome, OSA.*

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Introduction

In developmental age, the syndrome named as Attention Deficit Hyperactivity Disorder (ADHD) is characterized by inattention, hyperactivity, impulsivity, or a combination of these symptoms, compromising basic everyday functions such as learning abilities, executive functioning, and social skills[(1)].

Since the first description in 1902 by George Still on Lancet journal, the prevalence studies have reported different prevalence rates ranging 3% -5% of school-age children, and around 1% in Italian pediatric population[(2)].

To date, diagnostic criteria are based focus on behavioral symptoms, because the absence of specific biomarkers, although genetic factors, environmental factors, prematurity, low birth weight and hypoxic-ischemic encephalopathy are considered important in ADHD etiology. In this light, the role of sleep disorders may be an interesting and to date not yet well considered as causative factor for

ADHD, despite of many and relevant scientific evidences[3]. In fact, sleep disorders may be considered as a not secondary underlying cause of ADHD[3], although still underdiagnosed in pediatric age. On the other hand, there is growing evidence that sleep disorders and mainly the obstructive sleep apnea syndrome (OSA) are associated with behavioral problems and hyperactivity, executive functions impairment, cognitive and learning difficulties[4-13].

Starting from the frequent over-diagnosis among Italian children, the aim of the present study is verifying the presence of ADHD-like symptoms in other frequent condition such as sleep-related breathing disorders in pediatric age.

Material and methods

34 children (19 males and 15 females) aged 6-10 years (mean age 9.706 ± 3.434) with polysomnographic diagnosis of OSA, according to ICSD-3 criteria (14), were recruited.

Exclusion criteria were the following: overweight, obesity, cognitive disability (IQ <70), borderline intellectual functioning, neurological and psychiatric disorders (15-17), chromosomal defects, specific neuropsychological disorder, epilepsy[18-31].

Control group was composed by 89 typical developing children (47 males, 42 females) (mean age 9,528 ± 3,351).

All subjects of both groups were recruited within the same urban area, all were Caucasian and homogeneous for socioeconomic status

Ethical approval from the local Research Ethics Center and informed parental consent were obtained.

Polysomnographic (PSG) Data

After reviewing and analyzing PSG data collected from inpatients children between January and June 2016 to establish the presence of OSA in the experimental group, OSA severity was determined according to the current guidelines specified by the American Academy of Sleep Medicine (AASM)[32]: mild OSA was defined by an obstructive apnea-hypopnea index (o AHI) of 1 to <5 events per hour; moderate OSA was defined as was defined as ≥5 to <10 events/hour, and severe OSA ≥10 events/hour.

Conners' Rating Scale-Revised (CRS-R)

At the clinic visit, Conners' Rating Scale-Revised (CRS-R) was administered to mothers to assess their children's behavior. CRS-R examines seven types of behavior problems in children including: Oppositional, Anxious-Shy, Cognitive Problem/Inattention, Hyperactivity, Perfectionism, Psychosomatic, and Social Problems. It also contains four index scores: Conners' ADHD Index; Conners' Global Index (CGI): Restless-Impulsive; CGI: Emotional Lability; and CGI: Total. CRS-R also includes scales for the Diagnostic and Statistical Manual of Mental Disorders, 4th Edition[33] diagnosis of ADHD:

a) DSM-IV: Inattentive,
b) DSM-IV: Hyperactive-Impulsive,
c) DSM IV: Total.

Higher scores indicate an increased likelihood that a child would meet diagnostic criteria for ADHD. A T-score of 65 indicates a "clinically significant problem"[34].

Statistical analysis

For comparison between the two groups (OSAS and controls) it was applied t- testing and Chi-square test, where appropriate. P values<0.05 were considered statistically significant.

For statistical analysis it used the software STATISTICA (data analysis software system, version 6, StatSoft, Inc. (2001). For the comparison between the groups the t-test was applied. P values<0.05 were considered statistically significant.

Results

The two groups are comparable for age (p = 0.794) and sex distribution (p = 0.918). Subjects affected by OSA present higher scores in pathological range than controls in the following domains: hyperactivity, ADHD Index, Restlessness-impulsivity (CGI II), emotional instability (CGI IE), Hyperactivity and other problem areas (CGI T), DSM-IV inattention, DSM -IV hyperactivity and impulsivity, total DSM-IV ADHD, No. Inattention symptoms of DSM-IV, no symptoms of hyperactivity / impulsivity DSM-IV (p <0.001 for all subscales) (Table 1).

Discussion

Several studies have focused on alterations of executive functioning in children with OSA, with a putative specific relationship with the degree of respiratory troubles, supporting the role of intermittent hypoxia impact the fronto-prefrontal regions[6,7,10,35].

Considering the more relevant and frequency of OSA respect of ADHD (27% vs. 3-5%) in pediatric age, it is obvious and intuitive that hyperactive school-aged children may be affected by OSA more probable than ADHD.

	OSA N=34	Controls N=89	p
Oppositional	51.02±8.14	49.96±9.03	0.551
Cognitive Problem/Inattention	45.13±6.12	43.01±8.05	0.168
Hyperactivity	71.31±4.18	44.15±6.34	<0.001
Anxious-Shy	40.73±2.17	39.96±2.83	0.155
Perfectionism	46.93±9.15	44.18±8.93	0.132
Social Problems	50.37±7.39	50.93±7.25	0.704
Psychosomatic Problems	50.15±5.03	49.82±5.44	0.759
Conners' ADHD Index	77.36±10.04	45.26±6.19	<0.001
Restless-Impulsive (CGI I-I)	71.86±9.93	44.64±5.61	<0.001
Emotional Lability (CGI I-E)	59.05±6.94	45.11±7.09	<0.001
Hyperactivity and other problems (CGI T)	70.48±9.81	44.25±6.33	<0.001
DSM-IV Inattention	70.66±8.96	49.29±5.90	<0.001
DSM-IV Hyperactivity	75.71±8.83	49.63±4.31	<0.001
DSM-IV ADHD Total score	75.04±10.25	48.06±6.38	<0.001

Table 1: Shows differences between children affected by obstructive sleep apnea syndrome (OSA) and typical developing subjects among Conners Rating Scales-Revised version (CRS-R) scales. For comparison between the two groups (OSAS and controls) it was applied t- testing and Chi-square test, where appropriate. *P values<0.05 were considered statistically significant.*

In general, hyperactivity presents higher prevalence as non-specific symptom in several nosographic paintings of childhood neuropsychiatric interest, as a result of a reduction in inhibitory control both motor and behavioral skills. In fact, hyperactive and inattentive behavior has been reported in children with OSA and habitual snoring. In addition, children with higher indices of snoring tend to show lower scores to cognitive and neuropsychological standardized tests. On the other hand, in 2011 a systematic review has shown that the prevalence of OSA in ADHD subjects (25-30%) is higher than that of the general population (about 3%)[36]. In this perspective, the present study has as preliminary investigation in the evaluation of hyperactive behavior in school-aged children with OSAS.

Conversely, sleepy children tend to use a greater motor activity pattern to be more vigilant, supporting the parents' report about that when they are very tired appear angry and become aggressive and hyperactive. In this light, the use of stimulant drugs increase the catecholamines activity in the CNS, improving arousal and alertness in typical developing children, identifying it as the best treatment in ADHD to limit motor hyperactivity[27-29].

Moreover, the hypothesis that OSA may represent one of the causes of ADHD is supported by AASM guidelines that recommend screening for sleep apnea among children undergoing evaluation for ADHD[40], because of the overlapping cognitive, neuropsychological and behavioral symptoms and OSA.

In conclusion, scientific and clinical evidences tend to stress the similarities between ADHD and OSA effects/comorbidities in pediatric age, suggesting sleep screening as mandatory before starting stimulant drugs treatment[41-50].

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Review

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Pollution, the thyroid and neurodevelopment

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Abstract

The global prevalence of neurodevelopmental diseases is on the rise. The number of autistic babies in the US has jumped from 1 in 68 to 1 in 42. Plus more and more children have attention disorders or hyperactivity disorders. The genetic causes of these disorders of neurological development cannot explain such radical increases in the incidence and this leads one to look for the culprit in other elements, many of which have been shown to disrupt normal thyroid function. For instance, many polluting chemical substances can interfere with thyroid hormone (TH) metabolism and this might lead to abnormalities in the neurological development of the fetus or the child. ***Clin Ter 2016; 167(6):191-197. doi: 10.7417/CT.2016.1972***

Key words: *pregnancy, pollution, thyroid*

Introduction

The global prevalence of neurodevelopmental diseases is on the rise. The number of autistic babies in the US has jumped from 1 in 68 to 1 in 42. Plus more and more children have attention disorders or hyperactivity disorders. The genetic causes of these disorders of neurological development cannot explain such radical increases in the incidence and this leads one to look for the culprit in other elements, many of which have been shown to disrupt normal thyroid function. For instance, many polluting chemical substances can interfere with thyroid hormone (TH) metabolism and this might lead to abnormalities in the neurological development of the fetus or the child. To date, over 100 natural or synthetic substances have been reported to impact thyroid function. Since activity of this gland is essential for normal development in the uterus and during infancy, any alteration of the thyroid is of particular interest for pregnant women and for the newborn (1).

Thyroid diseases include benign ones, which from a functional standpoint can be attributed to normo- hypo- and hyperfunctioning forms (based on the amount of thyroid hormones produced), inflammatory diseases and neoplastic diseases.

The incidence of thyroid cancer has progressively risen in the last twenty years, as many cancer registries have shown. The data of the Surveillance, Epidemiology and End Results (SEER) Program Cancer Registries in the United States points to an annual increase over 5% from 1975-2002.(2) In Italy, from 1991-2005 the incidence of cancer – especially papillary – of the thyroid, has doubled, jumping from 8 to 18 new cases per year every 100,000 women and from 3 to 6 cases per year every 100,000 men (3,4).

The thyroid can also be affected by other diseases: goiter, hypothyroidism, hyperthyroidism, autoimmune diseases and these are also on the rise (5).

Having homogeneous data for statistical comparison is very difficult for various reasons; for example, the data extracted from screening programs conducted in even large samples in the US have clearly underscored a difference in the frequency of thyroid diseases in different ethnic groups. Even where the screening is done in otherwise homogeneous populations data can be dishomogeneous. For example the volcanic area of Etna in Italy is characterized by a high incidence of thyroid cancer; concentrations of various trace elements and heavy metals are significantly higher in the water and in the urine of its residents. This association is consistent with, but not confirmatory of, a cause and effect relationship between one or more chemical substances of volcanic origin and thyroid cancer (6).

Some of the causes considered to bring about this increase in thyroid diseases are: low iodine intake, especially in pregnancy and breastfeeding, genetics, medications, pollution, and new, more sensitive diagnostic methods. Polluting substances affect the thyroid and therefore neuro-

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development in the following main ways: by inhibiting the uptake of iodine into follicular cells, competing with THs at the receptor sites, displacing tetraiodiothyrosine (T4) from the transretinal transport protein, inhibiting thyroid peroxidase (TPO), reducing hormone half life through enzyme activation. Thyroid hormones are involved mainly in late events of neural development, such as migration and terminal differentiation of neurons and glia. However, thyroid hormones have been reported to affect proliferation and differentiation of neural precursors in the embryonic neurogenic regions during tadpole premetamorphosis or in studies investigating the effects of maternal thyroid hormone deficiencies. Intriguingly, progenitor proliferation in the embryonic subventricular zone (SVZ) leading to neocortex expansion is under T4 control through the integrin αvβ3 membrane receptor (7).

Thyroid pathophysiology: background

The thyroid is an endocrine gland that produces two hormones and to accomplish this it needs iodine and selenium. The World Health Organization estimates that iodine deficiency is one of the most severe public health issues, which translates into various diseases of greater or lesser severity depending on age and sex, such as hyper or hypo TH production by the gland. Iodine deficiency, and subsequent TH deficiency during fetal and neonatal development can have various effects including irreversible defects of brain maturation with severe consequences including mental retardation, deaf-mutism, and spastic paralysis. In its most severe forms iodine deficiency can lead to cretinism, a condition rarely found in Europe, where there remain pockets of moderate iodine deficiency resulting in minor cognitive and neuropsychological deficits (8,9).

The thyroid produces two hormones: tetraiodothyronine (T4) and triiodothyronine (T3) of which the essential component is iodine. When ingested with food, iodine is absorbed via the small intestine; from there it makes its way through the plasma to the thyroid, which absorbs it rapidly. In healthy adults about 90% of it is usually absorbed and its half life lasts about 12 hours; the remainder is expelled through the urine. Iodine trapping is the first step in the process through which it is metabolized in the thyroid. This is accompanied by the synthesis of thyroglobulin (Tg) and both phenomena are stimulated by thyroid stimulating hormone (TSH) produced by the pituitary. The process starts with the uptake of iodine from the capillary into the follicular cell by way of an energy-dependent active transport system driven by an electrochemical gradient and mediated by a sodium iodide symporter (NIS) protein whose expression on the follicular cell membrane is strongly regulated by plasma iodine levels in that low iodine levels increase the amount of NIS and thus iodine uptake, while the opposite occurs if the quantity of iodine is high. NIS alterations can play a crucial part in determining thyroid disorders and in particular autoimmune thyroid diseases (10). Once in the follicular cell, iodine is transported to the apical side of the cell membrane by a protein called pendrin, encoded by a known gene (the PDS gene) and whose impaired synthesis induces Pendred syndrome (11). Once at the apical side of the follicular cell, iodine incorporates into tyrosine residues of Tg by way of a reaction called iodine organification which is catalyzed by TPO. Transcription of the TPO gene is controlled by TTF-1, TTF-2 and PAX-8 genes, the very same transcription factors that regulate Tg, NIS and the TSH receptor (TSHR). (12) Coupling of the two iodotyrosine residues yields iodothyronines which are then stored in the colloid. Iodine organification can be inhibited by propylthiouracil (PTU) and by methimazole (MMI). The expression of NIS in normal or pathological tissues has been studied by using mono or polyclonal antibodies, which has shown that its expression increases 3-4 fold in basedowian tissue compared to normal tissue; this increase is sustained by high levels of anti-TSH receptor antibodies. In chronic autoimmune thyroiditis NIS expression is normal. With regard to malignant tumors, there is a reduced NIS level correlated to the reduced expression of the TSH receptor; anaplastic carcinoma is characterized by a loss of expression of the NIS gene. Notably, a defective iodine trapping mechanism leads to heterogeneous clinical presentations, especially in terms of the severity of goiter and hypothyroidism. This clinical polymorphism suggests that the phenotypic expression of the genetic defect correlates with other exogenous factors playing a significant role in the clinical expression of the disease.

Newly synthesized Tg is transfered by exocytic vesicles toward the apical membrane of the follicular cell, where iodination occurs, and is then stored in the follicular lumen. Thereinafter the iodinated Tg returns back into the cell through endocytic vesicles, migrating toward the basal membrane. Proteolytic enzymes inside the vesicles release T3 and T4 hormones. Even though the biologically active form is T3, it is calculated that most of the hormone excreted is T4 (80%). The latter of which is then transformed into T3 by way of three deiodinase enzymes, D1, D2 and D3, which contain selenium. Mercury, one of the most common polluting substances, can interfere with deiodinases and inhibit them. The affinity of T3 for thyroid hormone receptors (THRs) is 10 times stronger than that of T4. THRs are members of the nuclear receptor family and are encoded by two genes: THRA and THRB. Another enzyme, TPO, plays an important role in the thyroid, in that it protects thyroid cells from H_2O_2 damage that can arise during thyroid hormone synthesis (13). However, due to its high affinity for heavy metals such as cadmium and mercury it can be implicated in mercury poisoning. Symptoms of methyl mercury poisoning express themselves on the nervous system and its development.

Ontogenesis of thyroid function

The brain possesses a vast number of cells of various types and expresses 75% of the genes identified in man. Nearly all cells express thyroid hormone (TRα,Trβ, trϒ) receptors through which they regulate development of various types of neurons. Upon hormone binding, TRs regulate transcriptional genes including those involved in cell division, differentiation into specific types of neurons, formation of synapses and neural plasticity. It is therefore obvious that thyroid hormones are indispensable for normal fetal and infant brain development.

The thyroid is the earliest endocrine gland structure that appears during the morphogenic development of mammals. Differentiation into follicular structures containing colloid is observed already at 12 weeks in embryos. Thyroglobulin (Tg) synthesis is observed in the fetus after only 74 days of conception, while the incorporation of iodine into Tg starts only thereafter. The first phases of thyroid development seem to be independent of the pituitary but influenced only by thyroid stimulating hormone (TSH) secreted by the fetus itself; it has been found that the placenta is practically impermeable to maternal TSH. Even the quantity of T4 and T3 that from maternal circulation cross the placental barrier is irrelevant and in any case insufficient for ensuring normal embryo development. Therefore embryogenetic differentiation of the fetus is largely dependent on its hormone production and is independent of the hypothalamic–pituitary axis that is completed only later. In most animal species, and most likely in humans, inorganic iodine is, however, transfered from the mother to the fetus. Normal TH production is essential for normal neuronal migration and for myelination of the brain during fetal life and postnatally. A TH deficiency during these critical phases causes irreversible brain damage whose severity depends on both the time of exposure and the severity of the hypothyroxinemia (13). Pre-term newborns (>32 weeks) often manifest brain disorders that come to light at school, at about 5-6 years of age. Transient low T3 and T4 levels are characteristic in these newborns and this has been associated with the cognitive disorders found in these children.

The hypothalamus and pituitary, which are strongly interrelated and contribute to the synthesis of thyroid hormones, start developing in the fifth or sixth week of pregnancy.

The effects of two chemical pollutants have been explored: tetrabromobisphenol and tributyltin. These two substances bring on evident obesity in that TRH also has the ability to stimulate formation of adipose tissue by stimulating leptin. Numerous genes that produce NIS, TPO, DUOX2 (an oxidoreductase, which is functionally associated with TPO), DEHAL and the *TSHR* gene are implicated in TH synthesis. Since so many genes are involved, a large number of substances also interfere with thyroid metabolism in various ways. These are primarily perchlorates, widespread in water, which inhibit NIS or thiocarbamide-based medicines (used for hyperthyroidism), those with carbimazole, methimazole, and propylthiouracil, a TPO inhibitor. Bromine especially inhibits NIS, in the presence of iodine deficiency. It can be still found in the air due to the ongoing use of brominated flame retardants, has destructive effects on thyroid hormones. As bromine is even used as a leavening agent in the US, its disrupting effects on neurodevelopment can easily be imagined.

Cell Migration

Thyroid hormones exert an important influence on cell migration in the cerebral cortex, hippocampus and cerebellum. Among possible relevant mechanisms is an action exerted on the radial glia. The radial glia are derived from neuroepithelial cells that elongate as the embryonic brain epithelium thickens. These cells extend long processes to the cerebral wall, providing a scaffold that serves for cell migration. But they are not limited to a structural and supportive function. They are real stem cells that generate neurons and neuronal precursors, oligodendrocyte precursors, astrocytes, and ependymal cells. Radial glia maturation in the fetal rat brain is delayed in the hippocampus of hypothyroid rats, and this may affect migration of neurons, but may also impair neurogenesis. In the cerebral cortex, thyroid hormones are needed for the proper arrangement of the six-layer pattern, formed by the timely migration of cells originated in the ventricular neuroepithelium. Deficiency of thyroid hormone during the period of cortical development leads to less defined cortical layers, due to disturbances of cell migration. One mechanism by which thyroid hormones may influence neuronal migration in the cerebral cortex is through the regulation of the expression of the *Reln* gene (14).

Myelination

Hypothyroidism causes delayed and poor deposition of myelin whereas hyperthyroidism accelerates myelination. After prolonged neonatal hypothyroidism, the number of myelinated axons in adult rats is abnormally low in hypothyroid animals although most of the myelinated axons appear to have a normal thickness of the myelin sheath.

Thyroid hormones exert important effects on differentiation of oligodendrocytes, the cells that produce myelin. During development, hypothyroidism delays oligodendrocyte differentiation and myelin gene expression, eventually becoming normal even in the absence of thyroid hormone treatment. However, the myelination defect remains in adult animals, although oligodendrocytes are not targets of thyroid hormones in the adult. It is likely that the effects of thyroid hormones on myelination are mediated by another mechanism, i.e. their influence on axonal maturation. Axonal maturation is impaired in hypothyroidism, and the lower diameter of axons in hypothyroid animals would prevent many axons from reaching the critical size to become myelinated (15).

Sources of thyroid hormone for the fetus

At least in the rat, the fetal brain is impermeable to T3, and all brain T3 derives from T4.

Maternal T4 crosses the placenta, and the fetal blood-brain barrier (BBB), generating T3 locally in the fetal brain. Maternal T3 crosses the placenta and reaches most fetal tissues, but not the brain. The reason why the rat fetal brain is not permeable to T3 is unknown, and is not due to low expression of the Mct8 transporter. In rat fetuses most brain T3 derives from T4, but in postnatal and adult rats, the brain T3 derives in part from the blood and in part from local T4 deiodination. In the absence of Dio2, brain T3 is about 50% of normal, indicating that each source contributes nearly equally to the brain T3 content (16). Before the onset of thyroid function the only source of fetal thyroid hormone is the maternal thyroid gland. Thyroid hormones are present in rat embryos as early as 3 days after implantation and in the fetus well before the onset of fetal thyroid gland function. During fetal development the proportion of

hormone in the fetus originating in the fetal gland increases, and that of maternal origin decreases, but in the at-term rat maternal T4 still accounts for about 17.5% of the fetal extra thyroidal thyroxine pool. In humans T4 is already present in the coelomic fluid in which the yolk sack floats, as early as the 6th gestational week. In the fetal brain, T4 and T3 are present in significant amounts by the 10th week after conception. At term, about 30-50% of T4 present in neonates is of maternal origin (17).

Expression and regional distribution of deiodinases

The deiodinases are enzymes, otherwise disseminated throughout the body, which have the task of transforming the T4 to T3 by removing one iodine ion. There are three types named Dio 1, Dio 2, Dio 3.The predominant deiodinases present in the brain are Dio2 and Dio3, products of the *Dio2* and *Dio3* genes respectively. Dio1 activity is prominent in the cerebellum. Deiodinases are membrane-anchored proteins. Dio2 resides in the endoplasmic reticulum with the catalytic site exposed to the lumen. Dio1 and Dio3 are anchored to the plasma membrane with the catalytic site exposed to the intracellular compartment. Early evidence suggested that Dio3 in the plasma membrane was oriented with its catalytic site exposed to the extracellular fluid, having easy access to extracellular iodothyronines. If this was so, then the high abundance of Dio3 in the fetal brain would provide a rapid mechanism of inactivation for the T3 directly entering the brain parenchyma from the circulation, explaining the apparent impermeability of the fetal brain to T3. However, there is evidence that iodothyronines need to be internalized in the cell in order to act as Dio3 substrates, indicating that the catalytic site is oriented towards the interior of the cell or that there is a rapid internalization of Dio3 into endosomes (18).

Dio2 and *Dio3* are expressed in different cells, *Dio2* in astrocytes and *Dio3* in neurons.

Astrocytes generate the active T3 from T4, whereas neurons degrade T4 and T3 to rT3 and T2, respectively. The significance of this pathway for the developing brain is unknown. In *Dio2*-expressing tissues, such as brain, brown adipose tissue, and pituitary, 50% or more of T3 derives from local T4 deiodination. In the adult rat brain as much as 80% of nuclear bound T3 is formed locally from T4. Dio2 activity in the rat fetal brain increases markedly by the end of pregnancy, with a parallel 18-fold increase of brain T3 despite little changes in the plasma. Dio2 activity increases in hypothyroidism, and is very sensitive to the administration of T4. In iodine deficiency the increased Dio2 activity tends to maintain normal T3 concentrations despite greatly reduced T4 concentrations in the plasma and the brain. T4 inhibits Dio2 activity by a non-genomic action at the post-translational level involving the actin cytoskeleton and the ubiquitin-proteasome pathway. Dio2 is also regulated at the mRNA level, but less importantly (19,20).

Dio3 inactivates thyroid hormones through inner ring deiodination. Dio3 activity is highest in the placenta and in fetal tissues and decreases after birth. In the human placenta, Dio3 activity is 200 times higher than Dio2 activity at all gestational ages.

The brain barriers

The passage of substances from blood to brain is restricted by the blood-brain barrier (BBB) and the blood-cerebrospinal fluid (blood-CSF). The BBB is formed by the endothelial cells of brain capillaries which are apposed by tight junctions, so that substances must leave the circulation and enter the brain parenchyma through transcellular transport. Surrounding the brain capillaries are the astrocytic endfeet. It has been proposed that astrocyte membranes do not completely cover the capillary surface, leaving patches of capillary wall in contact with interstitial fluid (21). Other studies show that the astrocytes cover the capillaries completely, leaving only narrow spaces for free diffusion (22). In any case T4 and T3 transported through the BBB could reach the astrocytes through their endfeet or be delivered directly to interstitial fluid through the spaces between the astrocytes.

The transport of thyroid hormone through the plasma cell membrane is facilitated by several classes of transporter proteins. The discovery that mutations in one of these transporters, the monocarboxylate transporter 8 (MCT8), cause a syndrome of severe neurological impairment and thyroid hormone abnormalities, provided definitive proof for their pathophysiological relevance. In 2003 it was shown that rat MCT8 was a specific TH transporter, which closely resembles the human transporter (21) and this allowed for various experiments to be done, although to date no adequate therapy has been found to compensate for the absence of MCT8. Membrane transporters for thyroid hormones belong to several families including the monocarboxylate (MCT) transporters MCT8 and MCT10 (*SLC16A2* and *SLC16A10* genes), the organic anion transporter polypeptides (OATP, especially OATP1C1, *SLCO1C1* gene), the large neutral amino acid transporters (LAT-1 and LAT-2, products of the *SLC7A5* and *SLC7A8* genes), and the sodium/taurocholate cotransporting polypeptide (SLC10A1, or NTCP). MCT8 and MCT10 are specific for the transport of iodothyronines, with a slightly higher affinity for T3 than for T4. MCT10 is a transporter for aromatic amino acids (tryptophan, tyrosine, phenylalanine), and also mediates the influx and efflux of thyroid hormones. MCT10 appears to have little relevance for thyroid hormone transport in the brain (22).

Thyroid hormone transporters have a wide range of tissue distribution, with overlapping patterns of expression for most of them. In humans and rodents MCT8 is strongly expressed in the endothelial cells of the brain microvessels forming the BBB, and in the apical border of the epithelial cells of the choroid plexus. It is also expressed in the membrane of astrocytes, tanycytes, neurons, and oligodendrocyte precursors.

Oatp1c1 is a T4 transporter, and differential expression of Mct8 and Oatp1c1 is important to understand differential T4 and T3 transport through the BBB. Mct8, which transports T4 and T3, is expressed in the endothelial cells of the BBB and in astrocytes, neurons, and oligodendrocyte precursors. It is also expressed in newly formed oligodendrocytes. Oatp1c1, a T4 transporter, is expressed preferentially in the endothelial cells of the BBB and in astrocytes. Mct8 and Oatp1c1 are also expressed in the choroid plexus. As mentioned earlier *Dio2* is expressed mainly in astrocytes.

Thyroid hormone receptors in the brain

In rats the nuclear thyroid hormone receptor protein, measured by T3 binding assays, is present in the brain at embryonic day 13.5-14, i.e. several days before onset of thyroid gland function. The receptor increases subsequently and reaches a maximum on postnatal day 6. Total brain receptor occupancy by the hormone increases in parallel with plasma and cytosol total and free T3 with a maximum of 50-60% on postnatal day 15 (23). At the mRNA level, all receptor isoforms are expressed in the brain. The predominant TR isoform is TRα1, widely distributed in the CNS from E14 to adulthood. From E19 to P0, TRα1 is present in the outer part of the cerebral cortex and hippocampal CA1 field. During the late fetal stage TRα1 becomes expressed in the piriform cortex, superior colliculus, and pyramidal layer of the hippocampus, and in the granular layer of dentate gyrus. In adult rats TRα1 expression is prominent in the cerebral cortex, cerebellum, hippocampus, striatum and olfactory bulb. The pattern of TRβ1 expression during development is different than that of TRα1, with restricted low expression during the fetal period, and increasing during the postnatal period and through adulthood. TRβ1 mRNA can be detected at E15.5 in the upper tegmental neuroepithelium. Between E17 and E20 only low levels are present in the brain, especially in the pyramidal layer of the hippocampus. On P0 a drastic increase occurs in the accumbens, striatum, and hippocampus. From around P7 TRβ1 also becomes expressed in the cerebral cortex. The patterns of expression of TRα1 and TRβ1 overlap, but in some cells, one of the isoforms is expressed preferentially. For example, in the cerebellum, differentiated granular cells express TRα1 while Purkinje cells express TRβ1 (24,25).

Thyroid hormones as a target for pollution

The thyroid is highly vascularized and therefore easily reached by pollutants. The essential causes of TH metabolism alteration are: inhibition of iodine trapping into the follicular cell by blockage of NIS, inhibition of thyroid peroxidase synthesis, binding with blood transporter proteins, alteration of deiodinases and receptors.

Thyroid gland function is strongly conditioned by the environment and by interference from exogenous factors that include many medicines as well as natural (iodine, selenium, an excess of sulfur compounds in the soil or food) or artificial environmental factors (iodine isotope fallout and ionizing radiation). Thyroid homeostasis regulation through iodine intake is a clear example of the genome-environment interaction (26). The synthesis and secretion of hormones are dependent on the availability of dietary iodine which in turn depends on the iodine content of the soil. The severe harm that existed in the previous century (cretinism) in areas of moderate iodine deficiency no longer occurs although there are still cases of minor intelligence disorders. A moderate deficiency mainly affects areas of perception and cognition but can also cause hyperactive tendon reflexes, strabismus, dyslalia, proximal limb spasticity. In the fetus, THs control the maturation of specific cell clones and the expression of different genes and maturation of interneuronal connection systems indispensable for normal development of motor and cognitive capacities. This is why pregnancy and the first years of life are the most critical moments for these occurrences which can be prevented with adequate intake of dietary iodine. Many nutritional substances can have an antithyroid action and have been defined as natural goitrogens. An example of a natural inhibitor has been reported by some authors, who found out that a vegetable of the brassicaceae family very commonly used in China contains an enzyme, myrosinase, which generates many compounds (ex: thiocyanates, nitriles, oxazolidines) inhibiting iodine trapping into the cell (27).

The list of similar natural substances is especially long. The chemical groups involved are organic sulfur substances such as thiocyanates, isothiocyanates, goitrin, disulfides; flavonoids such as polyphenols and polyhydroxy phenols, pyridines, esters and phthalate metabolites, polychlorinated and polybrominated biphenyls, polycyclic aromatic hydrocarbons, inorganic iodine (in excess) and lithium. Based on their mechanism of action these substances can be broken down into two large groups: with direct or indirect goitrogenic action. The first group includes some inhibitors of iodine transport into the thyroid cell, those which interfere with intrathyroid iodine oxidation and organification processes and those which interfere with hormone proteolysis, deiodination and release. The second group includes polychlorinated and polybrominated biphenyls which accelerate peripheral deiodination of hormones and soy, which, in addition to interrupting the enterohepathic circulation of thyroid hormones, also reduces iodination.

Much of Europe is affected by pollution by endocrine disruptors. Some polycyclic or polyhalogenated aromatic compounds that have been called into question for environmental pollution and some food additives should be taken into special account. Many synthetic compounds that include pesticides and industrial chemical compounds of varied use are considered endocrine disruptors (plasticizers, food additives, flame retardants, cigarette smoke byproducts, etc.). Industrial compounds include heavy metals (e.g. mercury, cadmium, lead), polycyclic aromatic compounds, polyhalogenated compounds, phenol, etc.

Various forms of THs can bind with one or more atoms per ring and chemists have found that phenyl rings can also bind with other halogens aside from iodine, such as chloride, fluoride, and bromide. The result is that a myriad of substances in the air chemically mimic THs. These substances can interfere with TH homeostasis, blocking or reducing or even amplifying their action. Both inhibition and amplification of THs are very worrisome in the neurodevelopmental phase when THs must act with very precise concentrations and timing. Fewer substances can act on TSH receptors in that they are highly selective.

Dioxins and polychlorobiphenyls: Polychlorobiphenyls (PCBs) are a broad group of highly persistent industrial derivatives with elevated toxicity; their structure closely resembles that of dioxin. PCB mixtures were once used in a wide range of applications. Their broad commercial use mainly had to do with their high chemical stability, including being non-flammable, as well as useful physical properties such as being **thermal and electric insulators.** New production of PCBs was banned in Europe in 1970,

even though it continued well into 1993. Many substances of this group, of which dioxin stands out, bind to a TRH transcription factor and involve a reduction in circulating TH levels resulting in increased TSH. Many epidemiological studies have not all pointed to the same conclusions, often because the PCB family is too vast. A first investigational study was conducted by Collins who administered PCBs to adult rats in 1977 and revealed a drop in T4 levels both during the treatment phase and for three subsequent years. Later on an analogous study on gestating rats was performed and yet again a drop in T4 was found in fetal plasma and in brain tissue. Lastly, it has been shown that some PCBs induce hepatic production of TRβ receptors that may boost the production of hepatic enzymes that can glycosylate THs. Many other studies, however, have pointed out that this may not be the only mechanism by which TH can drop.

Brominated flame retardants: brominated flame retardants (BFRs) have been used for years in various forms: electronics, plastics, varnishes, and in textiles as foams and padding or in rugs. Their action on TH production goes about via two mechanisms: interference with TH metabolism and inhibition of iodine uptake into follicular cells. This is because BFRs have a very similar structure to that of THs (28).

Hexabromocyclododecane (HBCD): this cannot be used as of 2015 in the European Union because it is very persistent and toxic, but its use continues – subject to permission – in electronics, protective clothing, furniture and some high-end fabrics. Many studies have shed light on the negative impact of HBCDs on the thyroid and on neurodevelopment. For example an important study showed the inhibitory effects of HBCD on transcription responses of T3 and dendrite cell development in cerebellar cultures (29).

Tetrabromobisphenol A (TBBPA) is a chemical compound used to increase thermal resistance (e.g. of plastics, computer frames, etc.). It started being used in 2003 and in toxicity tests it always proved to be negative. Today it is well established that TBBPA displaces T4 from transretin, the T4 transport protein, therefore it alters its metabolism or is sometimes associated with increased T3 (31). This data, confirmed by others, illustrate the negative effects of maternal and fetal exposure on neural proliferation and on development of the nervous system.

Perfluorinated compounds (PFCs) are a certain number of surfactants used for surface protection and which are of great industrial interest. They are found in coatings resistant to oil and water spills, such as in fast food cartons, floor waxes, firefighting foam, cookware, popcorn package coating, etc. Their diffusion is ubiquitous, and they have been found in various concentrations in breast milk, in the blood of mothers and newborns in Europe. PFCs have been associated with decreased T4 and increased TSH. Its action might be due to increased glycosylation in the liver and to the displacement of retinol (30).

Perchlorates: perchlorate acts by inhibiting NIS and thus blocking iodine trapping into the follicular cell and formation of THs. Perchlorate is a strong oxidant used in fireworks, cartridges, and airbags. Because it is extremely stable, it is very widespread in drinking water and cooking water. It is associated with high urinary iodine and TSH levels. The fact that it may cross into the placenta and block cerebral NIS is of particular interest and is fueling studies. Even epidemiological data point to inconsistent conclusions: in some studies children had thyroid dysfunction, whereas in others their hormone panel was normal (31).

Nitrates and thiocyanates: the use of nitrates in fertilizers in agriculture is especially widespread, thus they also pollute groundwater. The action of nitrates on the thyroid comes about by inhibiting NIS. Thiocyanates also inhibit iodine uptake and at high concentrations can interfere with iodine organification. Children exposed to nitrates usually have high TSH levels and an enlarged thyroid (32).

Antimicrobial triclosan and parabens: by virtue of their antimicrobial action they can be found in personal care products such as soaps, deodorants, toothpaste, mouth wash, body cream, and cosmetics. Many animals treated with these products have shown them to have an effect on the thyroid as well as on spermatogenesis. In fact, in adolescents a positive correlation has been found between triclosan and T3 but the mechanism of action of triclosan on the thyroid remains unclear.

Isoflavones: isoflavones inhibit TPO. In humans they are mainly ingested via food, in particular through soy products, peas, beans, peanuts, coffee and tea. In some regions, such as in Asia, their consumption is very high, and in the first decade of life babies can develop hypothyroidism and goiter, especially in the presence of iodine deficiency.

Pesticides: the term "pesticide" includes at least 47 base substances that can vary in their manufacture and in their distribution; therefore studying them is wrought with difficulty. Exposure to many pesticides, starting with DDT, up to some still being used, such as hexachlorocyclohexane, usually arises from ingestion. Traces of these products have also been found in breast milk and cross through the placenta. Some of these, such as hexachlorobenzene act by destroying THs. High dichlorodiphenyldichloroethylene levels in the first trimester of pregnancy have been associated with a significant reduction in the neurodevelopment of children (33). Two recent studies have linked autism or a low intelligence coefficient to prenatal exposure to pesticides. Most of these substances exert their pesticide action by inhibiting acetylcholinesterase (ACE); given the role of ACE in neurotransmission during gestation, as well as in adults, it should not come as a surprise that they contribute to increased disorders such as autism (34-39).

Conclusions

The literature on thyroid disrupting effects of individual chemicals is rapidly increasing, as animal exposure studies and in vitro tests reveal a multitude of potential mechanisms of action. Although there is no currently available way to predict the effect of a complex body burden of thyroid disrupting chemicals in an individual patient, increased support from the medical community and from medical societies would be needed for a much more thorough evaluation of environmental exposure when thyroid disease is present.

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CASE REPORT

First evidence of HERV-H transcriptional activity reduction after methylphenidate treatment in a young boy with ADHD

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SUMMARY

Human endogenous retroviruses (HERVs) have been associated with many complex diseases including neuropsychiatric diseases, such as attention deficit hyperactivity disorder (ADHD). In ADHD an over-expression of HERV-H family in peripheral blood mononuclear cells has been documented. It has been hypothesized that HERVs may represent the link between genetic and environmental risk factors, contributing to the clinical onset and/or to the progression of the neurodevelopmental disease. The effect of pharmacological treatment on HERV transcriptional activity in psychiatric disorders has been attracting attention.

Using a real-time RT-PCR we investigated the influence of methylphenidate on HERV transcription in peripheral blood mononuclear cells of a young patient with ADHD.

In this clinical case we describe for the first time the reduction of HERV-H expression and the significant improvement of ADHD symptoms after 6 months of methylphenidate treatment

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INTRODUCTION

Several lines of evidence suggest that human endogenous retroviruses (HERVs) are associated with many complex diseases with multifactorial etiology and genetic basis, including neurological and psychiatric diseases. Up-regulation of transcriptional activity of some HERV sequences was found in schizophrenia, bipolar disorder (Perron *et al.,* 2012), autism spectrum disorders (Balestrieri et al., 2012) and attention deficit hyperactivity disorder (ADHD) (Balestrieri *et al.,* 2014). ADHD is one of the most common neurodevelopmental disorders, with onset in early childhood, strong heritability and documented brain abnormalities, whose etiology is probably the result of a complex interaction of genetic, biological and environmental factors (Curatolo *et al.,* 2009; Pluess *et al.,* 2005). Recently, we described for the first time an over-expression of the HERV-H family in peripheral blood mononuclear cells (PBMCs) from 30 drug-naïve children with ADHD (Balestrieri *et al.,* 2014) compared with healthy children. HERVs represent about 8% of the human genome (IHGC, 2001) and are part of the superfamily of repeated and transposable elements endowed with the ability to integrate into any location of the genome, altering the structure and/or function of other genes (Bannert and Kurth, 2001; Rowe and Trono, 2011). Elevated levels of HERV transcripts have been detected in brain tissues, cerebrospinal fluid and blood from patients with psychiatric disorders such as schizophrenia (Perron *et al.,* 2012). These patients are treated with drugs known to influence gene expression by inducing epigenetic modifications. The analysis of the HERV transcription pattern of human brain cell lines treated with various concentrations of valproic acid and neuroleptic drugs suggests that these medications may contribute to modify the expression of distinct HERV families (Diem *et al.,* 2012). In our previous study, ADHD patients were all drug-naive, and therefore we can exclude the influence of pharmacological treatment on HERV expression. MPH is the most common drug treatment for children with ADHD because of its effect (0.8-1.0) in reducing ADHD symptoms (Banaschewski *et al.,* 2006). MPH inhibits the reuptake of dopamine and noradrenaline into the presynaptic neuron, increasing their concentrations in the extra-neuronal space enhancing neurotransmission (Anderson *et al.,* 2006). This effect may be responsible for the improvement in ADHD symptoms observed after MPH treatment. To date there are no available studies on the effect of methylphenidate (MPH) on HERV families' expression. This is the first clinical report describing the effect of MPH on HERV-H expression in a young drug-naïve patient with ADHD.

Key words:
ADHD, Human endogenous retroviruses, Methylphenidate.

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CASE REPORT

The patient is a 16 year-old male. He is the second child of a non-consanguineous healthy couple. His mother had an uneventful pregnancy and a spontaneous, uncomplicated delivery. The family history is unremarkable. The patient,

Table 1 - *CPRS-T scores (Cognitive symptoms/Inattention, Hyperactivity, ADHD index and Oppositional) and CGI-I and CGS-S scores before and after 6 months of MPH treatment.*
CPRS, Conners' Parents Rating Scales (Score ranges from a low-T score of 61 mildly atypical to above 70 markedly atypical); CGI-S, Clinical Global Impressions - Severity (1-normal; 2-borderline; 3-mildly ill; 4-moderately ill; 5-strongly ill; 6-seriously ill; 7-extemely ill); CGI-I, Clinical Global Impressions – Improvement (1-greatly improved; 2-much improved; 3-improved a little; 4-no improvement; 5-worsened a little; 6-much worse; 7-extremely deteriorated).

	Before MPH treatment	*After 6 months MPH treatment*
Cognitive symptoms/ Inattention	80	65
Hyperactivity	90	67
ADHD index	95	65
Oppositional	84	67
CGI-S	6	2
CGI-I	4	2

with a diagnosis of ADHD combined type, according to DSM-IV-TR criteria, has been treated with cognitive behavioral therapy since he was 12 years old. The patient and his parents consulted child psychiatrists to discuss a possible drug prescription because he continued to be highly distractable and exhibited a significant impairment in social and school functioning. The diagnostic assessment included medical history, IQ evaluation, and the K-SADS clinical interview to exclude other psychiatric disorders. The Conners' Parents Rating Scales (CPRS) were used to assess ADHD clinical symptoms. Symptom severity and clinical improvement of the patient were assessed with the Clinical Global Impression-Severity (CGI-S) and Clinical Global Impression-Improvement (CGI-I) scales. Clinical response to MPH was evaluated using the CPRS and the CGI. The clinical evaluation using DSM-5 criteria (APA, 2013), confirmed a severe form of ADHD (CGI-S=6; seriously ill). The patient was drug-naïve. The ECG, EEG, haemogram, renal, liver and thyroid functions tests were normal. Findings on physical examination were normal. The clinicians confirmed the diagnosis of ADHD and decided to prescribe MPH treatment. The patient and his parents gave their written informed consent for pharmacological treatment, and signed a written informed consent form for the study of HERV-H expression before and after 6 months of MPH treatment. MPH-immediate release was started at an initial daily dose of 10 mg in the morning and was rapidly increased to 20 mg daily in two doses, with a marked improvement of ADHD core symptoms. The T scores of the CPRS decreased significantly between the baseline and after six months treatment. CGI-S and CGI-I scores indicated that MPH led to a significant control of symptoms (*Table 1*). At baseline and after six months, the patient had a BMI of 19.

PBMCs from the patient's heparinized blood sample were analyzed immediately after collection, before and after 6 months of MPH treatment (*Figure 1*). The expression levels of the env sequence from the HERV-H family were quantitatively assessed by real-time RT-PCR. Briefly, 250 µg of DNase-treated RNA from PBMCs were reverse-transcribed and amplified using primers specific for the HERV-H family using SYBR Green chemistry. The housekeeping gene GUSB was used to normalize the results (Balestrieri *et al.,* 2012). Each experiment was completed with a melting curve analysis to confirm the specificity of amplification and the lack of non-specific comparative method.

The results obtained are shown in *Figure 1* as the relative expression calculated using the threshold cycle (Ct) comparative method and, as calibrator, the mean of 5 samples from HC, matched for age and sex. The transcriptional level of HERV-H was drastically reduced after the MPH treatment from 119.98 to 0.67, while the transcriptional level of HC was 1.057±0.53.

DISCUSSION

HERV activity seems to be implicated in the pathogenesis of many complex diseases characterized by multifactorial etiology and genetic basis, such as ADHD (Balestrieri *et al.,* 2014). It has been hypothesized that HERVs may represent the link between genetic and environmental risk factors, contributing to the clinical onset and/or to the progression of neurodevelopmental diseases.

In children with ADHD we demonstrated that HERV-H expression correlates with the core symptoms of the dis-

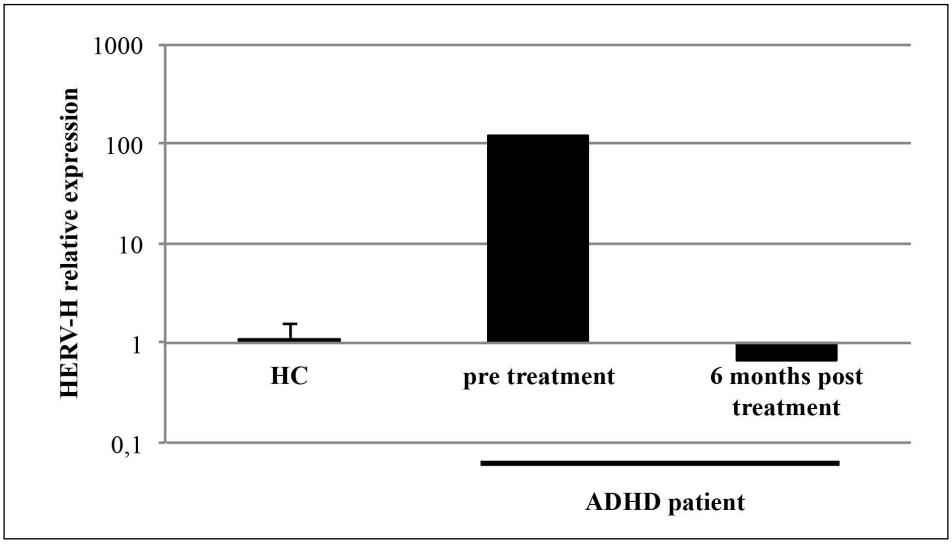

Figure 1 - *HERV-H relative expression before and after MPH treatment.*
The relative expression of HERV-H in an ADHD patient before and after methylphenidate treatment, compared with healthy controls was evaluated by real-time RT-PCR.

order (Balestrieri *et al.,* 2014). Recently, scientific studies demonstrated that pharmacological treatments may influence HERV expression, but no data are yet available on MPH treatment.

This case report describes for the first time the reduction of HERV-H expression in a young patient with ADHD after 6 months of MPH treatment, which determined a significant improvement of ADHD symptoms. This finding suggests that transcriptional activation of certain retroviral elements might be associated with the disease. HERVs have dynamic effects on gene function, and there are several potential mechanisms through which they can cause human disease (Diem *et al.,* 2012). A recent study demonstrated that the expression of HERV proteins increases the promoter activation of some genes, such as the dopamine receptor DRD3, and increases the expression of this gene in the neuroglia cells of patients with early onset schizophrenia (Huang *et al.,* 2011). Furthermore, more than 700 genes were upregulated in the striatum of MPH-treated rats. These genes are involved in the migration of immature neural/glial cells and/or growth of novel axons, in active axonal myelination, and in the upregulation of mature processes. Most of these genes are involved in a more enduring enhancement of neurobehavioral plasticity (Adriani *et al.,* 2006), through DNA methylation (Wu *et al.,* 2015).

Our finding suggests the possible role of HERVs in the pathophysiology of ADHD. The delineation of a role for retroviruses in disease pathogenesis might lead to new methods for the diagnosis and treatment of neurodevelopmental disorders. Future studies might investigate the expression of HERV families in patients with ADHD and correlate these findings with pharmacological treatment in a wider sample of ADHD patients.

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