

INDICE:

1. Dalle banche dati bibliografiche	pag.	2
2. Documenti		
Gagliano A, et al.		
A COMPARISON BETWEEN CHILDREN WITH ADHD AND CHILDREN WITH		
EPILEPSY IN SELF-ESTEEM AND PARENTAL STRESS LEVEL.		
Clin Pract Epidemiol Ment Health. 2014;10:176-83	pag.	67
D'Alatri L, et al.		
VOCAL FOLD NODULES IN SCHOOL AGE CHILDREN: ATTENTION DEFICIT HYPERACTIVITY		
DISORDER AS A POTENTIAL RISK FACTOR.		
J Voice. 2015 May;29:287-91	pag.	75
Loprieno U, Gagliano A.		
THE MEDIATING ROLE OF AGGRESSIVE BEHAVIOUR, EMOTIONAL AND BEHAVIOURAL INSTABILITY		
ON THE ASSOCIATION BETWEEN ADHD SYMPTOMS AND BEST FRIEND CONFLICTS.		
Minerva Pediatr. 2015 May	pag.	80
Lamberti M, et al.		
EVALUATION OF ACUTE CARDIOVASCULAR EFFECTS OF IMMEDIATE-RELEASE METHYLPHENIDATE		
IN CHILDREN AND ADOLESCENTS WITH ATTENTION-DEFICIT HYPERACTIVITY DISORDER.		
Neuropsychiatr Dis Treat. 2015;11:1169-74	pag.	107
Verkuijl N, et al.		
CHILDHOOD ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.		
BMJ 2015;350:h2168	pag.	113



teention it

isorder

N. 91 anno VI - maggio 2015

BIBLIOGRAFIA ADHD MAGGIO 2015

Acad Pediatr. 2015;15:282-88.

DIAGNOSIS OF ATTENTION-DEFICIT/HYPERACTIVITY DISORDER BY DEVELOPMENTAL PEDIATRICIANS IN ACADEMIC CENTERS: A DBPNET STUDY.

Feldman HM, Blum NJ, Gahman AE, et al.

Objective To describe the developmental-behavioral pediatricians (DBPs), patients, and clinical practices used in the diagnostic assessments of attention-deficit/hyperactivity disorder (ADHD) within all 12 academic medical centers comprising Developmental-Behavioral Pediatrics Research Network (DBPNet). **Methods** Between December 2011 and June 2012, all DBPs who evaluated children with ADHD or autism spectrum disorders were asked to complete a diagnostic encounter survey form for up to 10 consecutive new cases that resulted in the diagnosis of ADHD or autism spectrum disorder. Fifty-two clinicians returned one or more forms for children diagnosed with ADHD (n = 211).

Results DBPs were generally experienced full-time academics. Children were 76.3% male, 62.3% white, 24.5% African American, and 20.7% Hispanic. Mean child age was 8.0 + 3.1 years. DBPs reviewed parent ratings of behavior in 84.4% and teacher ratings in 69.2% of cases. They reviewed or completed at least one developmental assessment in 79.2% of cases: intelligence (60.2%), academic (57.8%), fine motor or visual motor (39.3%), speech/language (34.6%), or adaptive skills (28.9%). They made the diagnosis of coexisting conditions in 82.7% of cases, including learning disabilities (31.8%), speech/language disorders (31.8%), anxiety (14.2%), externalizing disorders (10.9%), and sleep disorders (9.5%). Among 146 children not medicated before the visit, stimulant medications were initiated in 15 children (10.2%).

Conclusions Within DBPNet, DBPs were highly likely to complete comprehensive assessments of ADHD that went beyond the requirements of primary care practice guidelines. They typically identified coexisting developmental and learning conditions. They did not typically prescribe medication at the end of diagnostic encounters.

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.

Accid Anal Prev. 2015 May;78:87-93.

THE IMPACT OF CHILDHOOD SYMPTOMS OF CONDUCT DISORDER ON DRIVER AGGRESSION IN ADULTHOOD. *Wickens CM, Vingilis E, Mann RE, et al*.

BACKGROUND: Despite limited empirical investigation, existing scientific literature suggests that individuals with a history or current diagnosis of conduct disorder (CD) may be more likely to demonstrate reckless and aggressive driving. Much of the limited research in this field examines the impact of childhood CD on driver behaviour and collision risk in young adults. Few if any, studies assess the impact of this disorder on driver behaviour beyond age 21 years. The current research is a population-based study of the impact of CD symptoms during childhood on the risk of engaging in driver aggression during adulthood.

METHODS: Data are based on telephone interviews with 5230 respondents who reported having driven in the past year. Data are derived from the 2011-2013 cycles of the CAMH Monitor, an ongoing cross-sectional survey of adults in Ontario, Canada aged 18 years and older. A binary logistic regression analysis of self-reported driver aggression in the previous 12 months was conducted, consisting of measures of demographic characteristics, driving exposure, problem substance use, alcohol- and drug-impaired driving, symptoms of attention deficit hyperactivity disorder, and childhood (before age 15) symptoms of CD.

RESULTS: When entered with demographic characteristics, driving exposure, and other potential confounders, childhood symptoms of CD increased the odds of reporting driver aggression more than two-fold (adjusted OR=2.12). Exploratory analyses of the interaction between childhood symptoms of CD and age was not a significant predictor of driver aggression.

CONCLUSIONS: Results suggest that symptoms of CD during childhood are associated with significantly increased odds of self-reported driver aggression during adulthood. Limitations and future directions of the research are discussed.

.....

Addiction. 2015 May;110:784-95.

DEVELOPMENTAL PROGRESSION TO EARLY ADULT BINGE DRINKING AND MARIJUANA USE FROM WORSENING VERSUS STABLE TRAJECTORIES OF ADOLESCENT ATTENTION DEFICIT/HYPERACTIVITY DISORDER AND DELINQUENCY.

Howard AL, Molina BSG, Swanson JM, et al.

Aims: To examine the association between developmental trajectories of inattention, hyperactivity– impulsivity and delinquency through childhood and adolescence (ages 8–16 years) and subsequent binge drinking and marijuana use in early adulthood (age 21 years).

Design: Prospective naturalistic follow-up of children with attention deficit/hyperactivity disorder (ADHD) previously enrolled in a randomized controlled trial (RCT). Treatment-phase assessments occurred at 3, 9 and 14 months after randomization; follow-up assessments occurred at 24 months, 36 months, and 6, 8 and 12 years after randomization.

Setting: Secondary analysis of data from the Multimodal Treatment Study of ADHD (MTA), a multi-site RCT comparing the effects of careful medication management, intensive behavior therapy, their combination, and referral to usual community care.

Participants: A total of 579 children with DSM-IV ADHD combined type, aged 7.0 and 9.9 years at baseline (mean = 8.5, SD = 0.80). Measurements Ratings of inattention, hyperactivity–impulsivity and delinquency were collected from multiple informants at baseline and through the 8-year follow-up. Self-reports of binge drinking and marijuana use were collected at the 12-year follow-up (mean age 21 years). Findings Trajectories of worsening inattention symptoms and delinquency (and less apparent improvement in hyperactivity–impulsivity) were associated with higher rates of early adult binge drinking and marijuana use, compared with trajectories of stable or improving symptoms and delinquency (of 24 comparisons, all P-values < 0.05), even when symptom levels in stable trajectories were high.

Conclusions: Worsening inattention symptoms and delinquency during adolescence are were associated with higher levels of early adult substance use; this pattern may reflect a developmental course of vulnerability to elevated substance use in early adulthood.

ADHD Atten Deficit Hyperact Disord. 2015.

THE ASSOCIATION OF EMOTIONAL LABILITY AND EMOTIONAL AND BEHAVIORAL DIFFICULTIES AMONG CHILDREN WITH AND WITHOUT ADHD.

Rosen PJ, Walerius DM, Fogleman ND, et al.

Children with ADHD often demonstrate a pattern of emotional lability characterized by sudden and intense shifts in affect. Emotional lability has been linked to emotional and behavioral problems in children with and without ADHD, but few studies have examined emotional lability over time. This study examined the effects of emotional lability over time on the behavioral and emotional difficulties of children with and without ADHD using an ecological momentary assessment (EMA) methodology. One hundred and two children aged 8null12 years (56 with ADHD and 46 without ADHD) and their parents completed baseline measures of the childrennulls behavioral and emotional difficulties. Parents then completed a 28-day 3-times daily EMA assessment protocol to rate their childnulls emotional lability. Results suggested that emotional lability was associated with internalizing and/or externalizing diagnoses independent of ADHD diagnostic status, but was not directly associated with ADHD. Hierarchical regression analyses supported ADHD diagnostic status as a moderator of the association of greater EMA-derived emotional lability with childrennulls behavioral difficulties, such that greater emotional lability was associated with greater behavioral difficulties among children with ADHD but not among children without ADHD. Results indicated that greater emotional lability was directly linked with greater emotional difficulties and that this relation was not moderated by ADHD diagnostic status. Overall, this study suggested that emotional lability is related to emotional difficulties independent of ADHD, but is differentially related to behavioral difficulties among children with and without ADHD.

Adolesc Psychiatry. 2015;5:73-83.

SUPPLEMENTS, DIETS AND OTHER COMPLEMENTARY AND ALTERNATIVE INTERVENTIONS IN ADOLESCENT MENTAL HEALTH.

.....

Bernstein B, Voll A.

Background: Complementary and alternative medicine (CAM) has become increasingly popular over the past 20 years and is used by many adolescents and their families. CAM includes a host of integrative approaches whose difference from traditional medicine center around its holistic rather than compartmentalized approach to the patient, in which evaluation of health and well-being considers the mind, body, and spirit.

Methods: This article provides an overview of both pharmacologic and non-pharmacologic approaches, with a focus on 1) how CAM can be used in clinical practice; 2) how to best choose amongst available approaches guided by research findings that provide information to maximize safety and efficacy. Two hypothetical cases illustrate how to apply the research base of evidence to patients and thus avoid diagnostic pitfalls and safety concerns.

Results: Current research points to the efficacy of CAM in adult and adolescent populations and the efficacy of interventions that include attention to good nutrition, regular exercise, sunlight, and hygiene, especially as these interventions may prevent or reduce the incidence of conduct disorder. Recent studies suggest that CAM treatments can improve overall functioning and reduce difficulties such as insomnia, depression and aggression that occur due to anxiety, attentional deficits, and mood disorders.

Conclusions: It is important to acknowledge the current public perception that CAM treatments are less likely to cause serious adverse effects as compared to conventional treatments. More studies of adolescent populations critical to confirm which complementary and alternative medicine treatments are both safe and efficacious. An informed open-minded attitude to non-conventional approaches has the potential to improve outcomes and trust amongst parents, adolescents and mainstream medical and behavioral health staff.

Adolesc Psychiatry. 2015;5:22-30.

TRANSITION FROM CHILDRENNULLS TO ADULT SERVICES FOR PATIENTS WITH ADHD: A MODEL OF CARE. *Moosa F, Sandhu T.*

Background: ADHD, a common childhood psychiatric disorder, is known to persist into adulsthood. Gaps and needs in the care of adolescents having ADHD when moving on from Childrennulls Mental Health Services (CAMHS) to Adult Mental Health Services (AMHS) exist and result in disruptions in care and lack of care. This report describes the outcome of a quality improvement project in Birmingham in the United Kingdom that focused on the patient journey and continuity of care.

Method: A CAMHS/AMHS transition (strategic) working group and a CAMHS ADHD transition (operational) team were set up. A validated dataset of those requiring transition was created and patient needs were reviewed. Planning and preparation for transition took place. The handover from CAMHS to AMHS was done at a joint clinic involving both services.

Results: Over a 12-month period, the number of patients on the waiting list for transfer from CAMHS to AMHS went from 134 to 14 and the waiting time for transition between the two services went from 12 months to four months. The referral rate for those in need of transfer from CAMHS to AMHS was optimised. The rate of successful handover (and transition) went from 18% to 55% after the introduction of the joint clinics.

Conclusion: A collaborative effort between CAMHS and AMHS, including the holding of joint clinics, ensured there was a comprehensive and effective transition care pathway in place for adolescents with ADHD.

.....

Adolesc Psychiatry. 2015;5:31-39.

PROMOTING WELL-BEING AND RESILIENCE IN EMPLOYING A RELATIONSHIP CENTERED APPROACH: A CASE STUDY OF A PRE-ADOLESCENT BOY.

Holder SM, Shoenleben R, Ellison-Daigneault R, et al.

Background: Relationship Centered Care (RCC) is a term that originated in the field of primary care, with roots in Engelnulls biopsychosocial model and humanistic medicine. It focuses on understanding of illness from an intersubjective perspective, involving a dialogue between physician and patient, and a shared understanding of the patientnulls narrative. The principles embodied in RCC have not been well described with respect to psychotherapeutic care with children and adolescents and their families, or in residential treatment settings, which may be hierarchical in their approaches.

Methods: This paper will demonstrate how employing multiple treatment modalities including (1) patient/ family, (2) shared decision making (3) emotional connections and (4) community partnerships, in using the Relationship Centered Care (RCC) approach can lead to the promotion of well-being and resilience. The case of a pre-adolescent boy with multiple mental health and behavioral issues will be used to illustrate this approach.

Results: The case demonstrates the effective utilization of the relationship-centered approach in comprehensively addressing the complex needs of a child with mental health and behavioral challenges.

Conclusions: The RCC approach helps bridge the coordination of multi-system plan of treatment intervention for a pre-adolescent youth in a childrennulls residential program yielding an optimal outcome for both the child and family.

.....

Am J Psychiatry. 2015 May;appiajp201514101266.

IS ADULT ADHD A CHILDHOOD-ONSET NEURODEVELOPMENTAL DISORDER? EVIDENCE FROM A FOUR-DECADE LONGITUDINAL COHORT STUDY.

Moffitt TE, Houts R, Asherson P, et al.

OBJECTIVE: Despite a prevailing assumption that adult ADHD is a childhood-onset neurodevelopmental disorder, no prospective longitudinal study has described the childhoods of the adult ADHD population. The

authors report follow-back analyses of ADHD cases diagnosed in adulthood, alongside follow-forward analyses of ADHD cases diagnosed in childhood, in one cohort.

METHOD: Participants belonged to a representative birth cohort of 1,037 individuals born in Dunedin, New Zealand, in 1972 and 1973 and followed to age 38, with 95% retention. Symptoms of ADHD, associated clinical features, comorbid disorders, neuropsychological deficits, genome-wide association study-derived polygenic risk, and life impairment indicators were assessed. Data sources were participants, parents, teachers, informants, neuropsychological test results, and administrative records. Adult ADHD diagnoses used DSM-5 criteria, apart from onset age and cross-setting corroboration, which were study outcome measures.

RESULTS: As expected, childhood ADHD had a prevalence of 6% (predominantly male) and was associated with childhood comorbid disorders, neurocognitive deficits, polygenic risk, and residual adult life impairment. Also as expected, adult ADHD had a prevalence of 3% (gender balanced) and was associated with adult substance dependence, adult life impairment, and treatment contact. Unexpectedly, the childhood ADHD and adult ADHD groups comprised virtually nonoverlapping sets; 90% of adult ADHD cases lacked a history of childhood ADHD. Also unexpectedly, the adult ADHD group did not show tested neuropsychological deficits in childhood or adulthood, nor did they show polygenic risk for childhood ADHD.

CONCLUSIONS: The findings raise the possibility that adults presenting with the ADHD symptom picture may not have a childhood-onset neurodevelopmental disorder. If this finding is replicated, then the disorder's place in the classification system must be reconsidered, and research must investigate the etiology of adult ADHD.

.....

ANN CLIN PSYCHIATRY. 2014;26:254-60.

ASTHMA IN PATIENTS WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER: A NATIONWIDE POPULATION-BASED STUDY.

Tsai C-J, Chou P-H, Cheng C, et al.

BACKGROUND: Asthma symptoms can interrupt daily activities, disturb sleep, and increase the risk of a child having an attention deficit or irritability, which also are symptoms of artention-deficit/hyperactivity disorder (ADHD). Previous studies have shown conflicting results regarding the association between ADHD and asthma. This study investigates the possible correlation between asthma and ADHD.

METHODS: We retrieved data on 221,068 pediatric patients from Taiwan's National Health Insurance Research Database in 2005, and calculated the prevalence and risk factors of allergic diseases among ADHD patients.

RESULTS: The prevalence of asthma in the ADHD group, compared with the control group, was 4.3 fold higher in the age 12 to 17 subgroup (95% CI, 1.71 to 10.6), 1.5-fold higher in males (95% CI, 1.05 to 2.03), and 1.6-fold higher for children living in urban areas (95% CI, 1.12 to 2.28). Multivariate logistic regression models showed the odds ratio of asthma for children with ADHD was 1.43 (95% CI, 1.05 to 1.95) as compared with children without ADHD.

CONCLUSIONS: Pediatric ADHD was associated positively with asthma, but the underlying mechanisms require further clarification

.....

Ann Gen Psychiatry. 2015;1-7.

THE EFFECT OF DIETARY EDUCATION ON ADHD, A RANDOMIZED CONTROLLED CLINICAL TRIAL.

Ghanizadeh A, Haddad B.

Background: The purpose of this research was to study the effectiveness of the overall dietary intervention rather than a single nutrient on children with attention deficit hyperactivity disorder (ADHD).

Methods: This is a randomized controlled trial conducted at a child psychiatry clinic in Iran. Participants were 106 children and adolescents with ADHD.

Results: The results revealed no significant difference between the two groups regarding mean age, gender ratio, body mass index, baseline inattentiveness score, and baseline hyperactivity score. Linear regression analysis considering the covariant variables showed that the inattentive score at the end of the trial was significantly associated with the mean change of favorite diet scores.

Conclusion: This is the first clinical trial examining the effect of overall dietary characteristics rather than a single nutrient on the children formally diagnosed with ADHD. According to the results, un-favorite diet had no effects on inattentive or hyperactivity/impulsivity score. Encouraging the children with ADHD to increase their intake of recommended diet markedly improves their attention.

Trial registration: The trial was registered at the Iranian Clinical Trials Registry (Irct ID: IRCT201311303930N29)

.....

Ann Neurosci. 2015;22:217-21.

LACK OF ASSOCIATION OF POLYMORPHISMS IN SIX CANDIDATE GENES IN COLOMBIAN ADHD PATIENTS. Fonseca DJ, Mateus HE, Galvez JM, et al.

Background: Attention Deficit and Hyperactivity Disorder (ADHD) is a common childhood neuropsychiatric condition. The disorder has a multifactorial background, with heritability estimates of around 76%, suggesting an important role of genetic factors. Candidate genes include those related to dopaminergic (e.g. DRD4, DRD5, SLC6A3 and DBH)and serotoninergic (e.g.HTR1B and SLC6A4) pathways. Purpose: To explore the association of common polymorphisms in six genes (DRD4, DRD5, SLC6A3, DBH, HTR1B and SLC6A4) and the susceptibility to ADHD in a Colombian sample population.

Methods: Eighty-six ADHD trios and 152 healthy controls were recruited. Genotyping of the six polymorphisms was performed using described PCR-based protocols. A TDT analysis was used to test if there was preferential allelic transmission for any of the six polymorphisms. Additionally, a case-control analysis was performed to test for association of the serotoninergic (HTR1B and SLC6A4) polymorphisms with ADHD.

Results: Through the TDT analysis there was no preferential allelic transmission for any of the studied variants. Case-control analysis did not show association.

Conclusion: This is the first study in Latin America to describe six polymorphisms in a group of patients with ADHD. There was no evidence of association for any of the studied polymorphic variants in this Colombian ADHD sample. Further research, with larger sample sizes and study of endophenotypes, is needed in this population to confirm and extend the results.

.....

Arch Toxicol. 2015 May;89:687-709.

DEVELOPMENTAL NEUROTOXICITY OF PERSISTENT ORGANIC POLLUTANTS: AN UPDATE ON CHILDHOOD OUTCOME. Berghuis SA, Bos AF, Sauer PJ, et al.

Organohalogens are persistent organic pollutants that have a wide range of chemical application. There is growing evidence that several of these chemical compounds interfere with human development in various ways. The aim of this review is to provide an update on the relationship between various persistent organic pollutants and childhood neurodevelopmental outcome from studies from the past 10 years. This review focuses on exposure to polychlorinated biphenyls (PCBs), hydroxylated PCBs (OH-PCBs), polybrominated diphenyl ethers (PBDEs) and dichlorodiphenyldichloroethylene (DDE), and in addition on exposure to phthalates, bisphenol A, and perfluorinated compounds and their associations with neurodevelopmental outcome in childhood, up to 18 years of age. This review shows that exposure to PCBs and OH-PCBs, most studies report no or inverse associations with neurodevelopmental outcomes. Regarding exposure to PBDEs, lower mental development, psychomotor development and IQ were found at preschool age, and poorer attention at school age. Regarding exposure to DDE, most studies reported inverse associations with outcome, while others found no associations. Significant relations were particularly found at early infancy on psychomotor development, on attention and ADHD, whereas at school age, no adverse

relationships were described. Additionally, several studies report gender-related vulnerability. Future research should focus on the long-term effects of prenatal and childhood exposure to these environmental chemicals, on sex-specific and combined exposure effects of environmental chemicals, and on possible mechanisms by which these chemicals have their effects on neurodevelopmental and behavioral outcomes.

.....

Atten Defic Hyperact Disord. 2015 Jun;7:157-64.

EFFECTIVENESS AND SAFETY OF A LONG-ACTING, ONCE-DAILY, TWO-PHASE RELEASE FORMULATION OF METHYLPHENIDATE (RITALIN((R)) LA) IN SCHOOL CHILDREN UNDER DAILY PRACTICE CONDITIONS. *Haertling F, Mueller B, Bilke-Hentsch O*.

Long-acting (LA) preparations of methylphenidate allow for once-daily dosing; however, pharmacokinetics may vary and depend on food intake. The objective was to evaluate effectiveness of a two-phase release formulation (Ritalin((R)) LA) under daily practice conditions. This was a prospective, multicenter, observational study in Germany. Eligibility and dosing were determined by the physician based on the drug label. Outcomes included changes over 3 months of treatment in assessments of effect duration, clinical global impression (CGI), and quality of life (ILK). In 101 sites, 262 patients (197 boys, 63 girls, and two unknown) with a mean age of 10.9 years were enrolled; 50 were treated for the first time; 212 switched medication to Ritalin((R)) LA. After 3 months, CGI improved in 59.4 % of patients, and well-being overall was rated as good by 61.0 % of parents and 63.7 % of children. Based on parents' assessment, the proportion of children suffering from strong disease burden decreased from 40.7 to 15.1 %. In 123 insufficient responders to previous ADHD medications, benefit from Ritalin((R)) LA was above average and effect duration was significantly prolonged as compared to pretreatment. Overall, 28 patients (10.7 %) had treatment-related adverse events with one case being serious; 23 patients (8.8 %) discontinued therapy, 7 (2.7 %) due to poor treatment response; and 212 patients (81 %) continued treatment beyond the study. In line with clinical trial data, Ritalin((R)) LA provides significant benefit also under routine practice conditions.

.....

Autism. 2015 May;19:400-08.

TEMPERAMENT AND CHARACTER AS ENDOPHENOTYPE IN ADULTS WITH AUTISM SPECTRUM DISORDERS OR ATTENTION DEFICIT/HYPERACTIVITY DISORDER.

Sizoo BB, van der Gaag RJ, van den Brink W.

Autism spectrum disorder and attention deficit/hyperactivity disorder overlap in several ways, raising questions about the nature of this comorbidity. Rommelse et al. published an innovative review of candidate endophenotypes for autism spectrum disorder and attention deficit/hyperactivity disorder in cognitive and brain domains. They found that all the endophenotypic impairments that were reviewed in attention deficit/hyperactivity disorder were also present in autism spectrum disorder, suggesting a continuity model with attention deficit/hyperactivity disorder as "a light form of autism spectrum disorder." Using existing data, 75 adults with autism spectrum disorder and 53 with attention deficit/hyperactivity disorder were directly compared on autistic symptoms with the autism spectrum quotient, and on the endophenotypic measure of temperament and character, using the Abbreviated (Dutch: Verkorte) Temperament and Character Inventory. Based on the hypothesis that attention deficit/hyperactivity disorder and autism spectrum disorder are disorders on a continuous spectrum, autism spectrum quotient scores and abbreviated Temperament and Character Inventory scores were expected to be different from normal controls in both disorders in a similar direction. In addition, the autism spectrum quotient and abbreviated Temperament and Character Inventory scores were expected to be closely correlated. These conditions applied to only two of the seven Abbreviated Temperament and Character Inventory scales (harm avoidance and self-directedness), suggesting that temperament and character as an endophenotype of

autism spectrum disorder and attention deficit/hyperactivity disorder provides only partial support for the continuity hypothesis of autism spectrum disorder and attention deficit/hyperactivity disorder.

.....

Autism Res. 2015.

MOTOR CIRCUIT ANATOMY IN CHILDREN WITH AUTISM SPECTRUM DISORDER WITH OR WITHOUT ATTENTION DEFICIT HYPERACTIVITY DISORDER.

Mahajan R, Dirlikov B, Crocetti D, et al.

This study examined the morphology of frontal-parietal regions relevant to motor functions in children with autism spectrum disorder (ASD) with or without attention deficit hyperactivity disorder (ADHD). We also explored its associations with autism severity and motor skills, and the impact of comorbid ADHD on these associations. Participants included 126 school-age children: 30 had ASD only, 33 had ASD with ADHD, and 63 were typically developing. High resolution 3T MPRAGE images were acquired to examine the cortical morphology (gray matter volume, GMV, surface area, SA, and cortical thickness, CT) in three regions of interest (ROI): precentral gyrus (M1), postcentral gyrus (S1), and inferior parietal cortex (IPC). Children with ASD showed abnormal increases in GMV and SA in all three ROIs: (a) increased GMV in S1 bilaterally and in right M1 was specific to children with ASD without ADHD; (b) all children with ASD (with or without ADHD) showed increases in the left IPC SA. Furthermore, on measures of motor function, impaired praxis was associated with increased GMV in right S1 in the ASD group with ADHD. Children with ASD with ADHD showed a positive relationship between bilateral S1 GMV and manual dexterity, whereas children with ASD without ADHD showed a negative relationship. Our findings suggest that (a) ASD is associated with abnormal morphology of cortical circuits crucial to motor control and learning; (b) anomalous overgrowth of these regions, particularly S1, may contribute to impaired motor skill development, and (c) functional and morphological differences are apparent between children with ASD with or without ADHD.

.....

Basic Clin Neurosci. 2015;6:45-54.

ATTENTION DEFICIT HYPER ACTIVITY DISORDER (ADHD) AND STRESS: A MUTUAL RELATIONSHIP BETWEEN CHILDREN AND MOTHERS.

Samiee M, Daneshmand R, Keramatfar R, et al.

Introduction: Attention Deficit Hyperactivity Disorder (ADHD) is a neurodevelopmental disorder characterized by high levels of inattention, hyperactivity and impulsivity which may result in mothers' stress. The current study aims to compare stress among 45 mothers of ADHD children who had referred to "Rofeydeh psychiatric center" with 45 mothers of normal children.

Methods: Brief demographic researcher-made questionnaire, Child Symptom Inventory-4 (CSI-4), the Child Behavior Checklist (CBCL), and Parental Stress Index-Short Form (PSI/SF) were completed for each mother and child.

Results: The results showed that except the component of acceptance, ADHD children had more problems in the field of attention compared with normal children. Mothers of ADHD children had also more stress compared with mothers of normal children.

Discussion: ADHD can impair mothers' mental health by inducing stress and this issue has important clinical and treatment implications. Specific treatment programs should be designed and implemented in Iran for the mothers of ADHD children to reduce stress among them and therefore, improve their mental health status.

Behav Brain Funct. 2015;11.

EVALUATING COGNITIVE AND MOTIVATIONAL ACCOUNTS OF GREATER REINFORCEMENT EFFECTS AMONG CHILDREN WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.

Fosco WD, Hawk LW, Rosch KS, et al.

Background: Attention Deficit/Hyperactivity Disorder is associated with cognitive deficits and dysregulated motivation. Reinforcement improves cognitive performance, often to a greater degree among children with ADHD compared to typically-developing controls. The current study tests the degree to which cognitive (individual differences in baseline cognition) and/or motivational (individual differences in Sensitivity to Reward; SR) processes can account for diagnostic group differences in reinforcement effects.

Methods: Participants were 58 children (25 ADHD, 33 control) ages 9-12. Children completed measures of inhibitory control (Stop Signal Task), working memory (n-back), and sustained attention (Continuous Performance Task) during a baseline week and again one week later under reinforcement and no-reinforcement conditions; composites were computed across cognitive domains. Parent-and child-reported trait SR (SPSRQ; BIS/BAS) were combined to index a child's response towards appetitive, rewarding stimuli.

Results: In separate analyses, diagnostic group, individual differences in baseline cognition, and individual differences in SR all moderated the impact of reinforcement on cognition. When considered together, the Diagnostic Group null Reinforcement and Baseline Cognition null Reinforcement interactions both remained robust. In contrast, neither the Diagnostic Group null Reinforcement nor the SR null Reinforcement interactions accounted for unique variance when evaluated together.

Conclusions: Both baseline cognition and trait SR predict reinforcement effects on cognition, but only SR shares significant variance with diagnostic group. These results suggest that ADHD children's greater response to reinforcement on cognition is strongly related to their heightened trait sensitivity to rewarding stimuli, consistent with motivational models of ADHD.

.....

Behavioural Processes. 2015 May;114:52-62.

COMPARING HYPERBOLIC, DELAY-AMOUNT SENSITIVITY AND PRESENT-BIAS MODELS OF DELAY DISCOUNTING. *Mitchell SH, Wilson VB, Karalunas SL*.

Delay discounting is a widely studied phenomenon due to its ubiquity in psychopathological disorders. Several methods are well established to quantify the extent to which a delayed commodity is devalued as a function of the delay to its receipt. The most frequently used method is to fit a hyperbolic function and use an index of the gradient of the function, k, or to calculate the area under the discounting curve. The manuscript examines the behavior of these quantification indices for three different datasets, as well as provides information about potential limitations in their use. The primary limitation examined is the lack of mechanistic specificity provided by either method. Alternative formulations that are thought to provide some mechanistic information are examined for the three separate datasets: two variants of a hyperbolic model (Rachlin, 1989, Judgment, decision and choice. New York: W.H. Freeman) and the quasi-hyperbolic model (Laibson, 1997, Q. J. Econ., 112, 443–477). Examination of the parameters of each formulation suggests that the parameters derived from the quasi-hyperbolic model allows groups and conditions within the three datasets to be reliably distinguished more readily than the hyperboloid models. However, use of the quasi-hyperbolic model is complex and its limitations might offset its ability to discriminate within the datasets.

.....

Biol Res Nurs. 2015 May;17:257-62.

SYMPTOMS OF ATTENTION-DEFICIT HYPERACTIVITY DISORDER, NONSYNDROMIC OROFACIAL CLEFT CHILDREN, AND DOPAMINE POLYMORPHISMS: A PILOT STUDY.

Hopkins EE, Wallace ML, Conley YP, et al.

PURPOSE: Attention-deficit hyperactivity disorder (ADHD) is a common childhood neurobehavioral disorder characterized by inattention, poor impulse control, and motor restlessness. Risk factors include familial stressors, anxiety disorders, learning disabilities, abnormal brain development, heritability, and

dopamine polymorphisms. Children with an orofacial clefting (OFC) history are at increased risk of familial stressors, anxiety disorders, learning disabilities, and abnormal brain development. Given this overlap, we present a conceptual model proposing that children with OFC may be more likely to exhibit ADHD symptoms than children without and explore this relationship using pilot data.

DESIGN: This cross-sectional pilot study included 29 children with OFC or a first-degree relative with OFC recruited through a cleft research registry.

METHODS: The Disruptive Behavior Disorder Scale was used to collect data on children's ADHD symptoms. Saliva or whole blood samples were collected from children and parents for DNA analyses. ADHD-associated dopamine polymorphisms within the DRD4, DRD2, and DAT1 genes were genotyped. We tested for associations between presence of OFC and dopamine polymorphisms. Mixed-effects models tested whether children with OFC and dopamine polymorphisms had more ADHD symptoms.

RESULTS: The DRD4 4-repeat allele was associated with increased inattentive ADHD symptoms (p = .03). Having the DRD2 Taq1A1 allele and OFC predicted fewer (p = .02) inattentive ADHD symptoms. Children with OFC were significantly less likely to have the DAT1 10-repeat allele (p = .04).

CONCLUSIONS: Results indicate that further investigation among a larger sample of children with OFC is warranted, particularly for relationships with inattentive ADHD.

.....

Biol Psychiatry. 2015;77:880-86.

ATTENTION-DEFICIT/HYPERACTIVITY DISORDER AND RISK FOR SUBSTANCE USE DISORDERS IN RELATIVES. Skoglund C, Chen Q, Franck J, et al.

Background: Previous research indicates that attention-deficit/hyperactivity disorder (ADHD) is highly associated with substance use disorders (SUD). However, these studies have failed to clarify the nature of the overlap. The main aim of this study was to explore whether the overlap between ADHD and SUD could be explained by shared genetic and environmental factors or by harmful effects of ADHD medication.

Methods: We employed a matched cohort design across different levels of family relatedness recorded from 1973-2009. By linking longitudinal Swedish national registers, 62,015 ADHD probands and first-degree and second-degree relatives were identified and matched 1:10 with control subjects without ADHD and their corresponding relatives. Any record of SUD was defined by discharge diagnoses of the International Classification of Diseases or a purchase of any drug used in the treatment of SUD.

Results: First-degree relatives of ADHD probands were at elevated risk for SUD (odds ratios 2.2 and 1.8) compared with relatives of control subjects. The corresponding relative risk in second-degree relatives was substantially lower (odd ratios 1.4 and 1.4). The familial aggregation patterns remained similar for first-degree and second-degree relatives after excluding individuals with coexisting disorders such as schizophrenia, bipolar disorder, depression, and conduct disorder.

Conclusions: Our findings suggest that the co-occurrence of ADHD and SUD is due to genetic factors shared between the two disorders, rather than to a general propensity for psychiatric disorders or harmful effects of ADHD medication.

.....

Biomark Insights. 2015;10:33-38.

POLYMORPHISM IN VARIABLE NUMBER OF TANDEM REPEATS OF DOPAMINE D4 GENE IS A GENETIC RISK FACTOR IN ATTENTION DEFICIT HYPERACTIVE EGYPTIAN CHILDREN: PILOT STUDY.

Shahin O, Meguid NA, Raafat O, et al.

INTRODUCTION: The variable number of tandem repeats (VNTR) of the dopamine receptor D4 (DRD4) gene among humans may elucidate individual differences in susceptibility to neuropsychiatric diseases. Dopamine dysfunction may be involved with Attention Deficit Hyperactivity Disorder (ADHD) symptoms. In this study, we report the association between the phenotype of ADHD, a condition characterized by inattentiveness, hyperactivity, and impulsiveness, and a 48-base pair VNTR in exon 3 of the DRD4 polymorphism.

SUBJECTS AND METHODS: We used a case control approach conducted on 29 ADHD and 31 ethnically matched control Egyptian children (ages 6-12 years). Cases were assessed by a psychiatric semistructured interview and the Conners' Parent Rating Scale. VNTR polymorphisms of the DRD4 gene were done by touchdown PCR program using exon 3-specific primers followed by agarose gel electrophoresis.

RESULTS: We observed a significant association between the existence of D4.4 allele of DRD4 and ADHD (P, 0.002); 6.9% of cases showed a single D4.4 and 10.3% showed a double D4.4 as compared to controls in whom D4.4 has never been detected.

CONCLUSION: Children with smaller number of repeat alleles (two to four repeats) of the DRD4 gene have higher possibility to develop ADHD in Egyptian children.

.....

Bipolar Disord. 2015;17:315-22.

COMORBIDITY OF ADHD AND SUBSEQUENT BIPOLAR DISORDER AMONG ADOLESCENTS AND YOUNG ADULTS WITH MAJOR DEPRESSION: A NATIONWIDE LONGITUDINAL STUDY.

Chen M-H, Chen Y-S, Hsu J-W, et al.

Objectives: Previous studies have found that attention-deficit hyperactivity disorder (ADHD) in childhood and adolescence is associated with an increased risk of major depression and bipolar disorder in later life. However, the effect of ADHD comorbidity on the diagnostic conversion to bipolar disorder among patients with major depression is still uncertain.

Methods: Using the Taiwan National Health Insurance Research Database, 58,023 subjects < 30 years of age who had major depression with (n = 1,193) or without (n = 56,830) ADHD comorbidity between the years 2000 and 2008 were enrolled in our study. Subjects who developed bipolar disorder during the follow-up to the end of 2011 were identified.

Results: Adolescents and young adults who had major depression with ADHD comorbidity had an increased incidence of subsequent bipolar disorder (18.9% versus 11.2%, p < 0.001) compared to those without ADHD. Cox regression analysis showed that ADHD comorbidity was an independent risk factor (hazard ratio = 1.50, 95% confidence interval 1.30-1.72) predicting subsequent bipolar disorder among those with major depression, adjusting for demographic data and psychiatric comorbidities.

Conclusions: Patients with comorbid diagnoses of major depression and ADHD had an increased risk of diagnostic conversion to bipolar disorder compared to those who had major depression alone. Further studies would be required to validate this finding and to investigate the possible underlying mechanisms.

.....

BMC Pediatr. 2015.

ATTENTION-DEFICIT/HYPERACTIVITY SYMPTOMS IN PRESCHOOL CHILDREN FROM AN E-WASTE RECYCLING TOWN: ASSESSMENT BY THE PARENT REPORT DERIVED FROM DSM-IV.

Zhang R, Huo X, Ho G, et al.

Background: To investigate the attention-deficit/hyperactivity disorder (ADHD) status among preschoolaged children in Guiyu, an electronic waste (e-waste) recycling town in Guangdong, China.

Methods: Two hundred and forty-three parents were surveyed regarding ADHD behaviors in their children (aged 3-7 years) based solely on the DSM-IV criteria. The peripheral blood samples were taken from these children to measure blood lead levels (BLLs) and blood cadmium levels (BCLs).

Results: 12.8% of children met the criteria for ADHD, of which the inattentive, hyperactive/impulsive and combined subtypes were 4.5%, 5.3% and 2.9% respectively. Of all children, 28.0% had BLLs (greater-than or equal to) 10 ug/dL and only 1.2% had BCLs (greater-than or equal to) 2 ug/L, levels conventionally considered high. Either modeled by univariate or multivariable analysis, the three ADHD scores (inattentive, hyperactive/impulsive and total scores) calculated from the Parent Rating Scale showed strong positive correlations with BLLs but not with BCLs. Furthermore, children with high BLLs had 2.4 times higher risk of ADHD than those with low BLLs (OR: 2.4 [95% CI: 1.1-5.2]). When each of the 18 categories on the Parent Rating Scale was separately analyzed, children with high BLLs had significant higher risks

for positive ADHD symptoms than those with low BLLs in 12 of the 18 categories (ORs ranged from 2.1 [95% CI: 1.1-3.9] to 3.6 [95% CI: 1.7-7.5]).

Conclusions: This study suggests that environmental lead contamination due to e-waste recycling has an impact on neurobehavioral development of preschool children in Guiyu.

.....

BMC Psychiatry. 2015;15.

IMPROVED QUALITY OF LIFE AMONG ADOLESCENTS WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER IS MEDIATED BY PROTECTIVE FACTORS: A CROSS SECTIONAL SURVEY.

Schei J, Novik TS, Thomsen PH, et al.

Background: The aim of this study was to assess the role of protective factors as mediators and/or moderators of the relationship between coexisting emotional and conduct problems and quality of life (QoL) among adolescents with attention-deficit/hyperactivity disorder (ADHD).

Methods: The sample consisted of 194 adolescents with ADHD. Participants completed measures of individual competencies, family cohesion and social support, and QoL. Coexisting emotional and conduct problems were assessed using the Strength and Difficulties Questionnaire.

Results: Individual competencies and social support mediated the association between emotional and conduct problems and QoL. Family cohesion was associated with both emotional and conduct problems. No moderating effects of protective factors and coexisting problems were found.

Conclusions: The assessment of individual competencies, social resources, and family cohesion may identify potential treatment goals for adolescents with ADHD and coexisting problems, and may contribute to improvements in QoL.

.....

BMJ. 2015;350:h2168. CHILDHOOD ATTENTION-DEFICIT/HYPERACTIVITY DISORDER. Verkuijl N, Perkins M, Fazel M.

.....

Child Care Health Dev. 2015 May.

THE EFFECTS OF PHYSICAL EXERCISE IN CHILDREN WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER: A SYSTEMATIC REVIEW AND META-ANALYSIS OF RANDOMIZED CONTROL TRIALS.

Cerrillo-Urbina AJ, Garcia-Hermoso A, Sanchez-Lopez M, et al.

OBJECTIVE: The aim of this systematic review and meta-analysis was to examine the evidence for the effectiveness of exercise interventions on attention deficit hyperactivity disorder (ADHD)-related symptoms such as inattention, hyperactivity/impulsivity, anxiety and cognitive functions in children and adolescents. **METHOD**: Five databases covering the period up to November 2014 (PubMed, Scopus, EMBASE, EBSCO [E-journal, CINAHL, SportDiscus] and The Cochrane Library) were searched. Methodological quality was assessed using the Cochrane tool of bias. Standardized mean differences (SMD) and 95% confidence intervals were calculated, and the heterogeneity of the studies was estimated using Cochran's Q-statistic. **RESULTS**: Eight randomized controlled trials (n = 249) satisfied the inclusion criteria. The studies were grouped according to the intervention programme: aerobic and yoga exercise. The meta-analysis suggests that aerobic exercise had a moderate to large effect on core symptoms such as attention (SMD = 0.84), hyperactivity (SMD = 0.56) and impulsivity (SMD = 0.56) and related symptoms such as anxiety (SMD = 0.66), executive function (SMD = 0.58) and social disorders (SMD = 0.59) in children with ADHD. Yoga exercise suggests an improvement in the core symptoms of ADHD. **CONCLUSIONS**: The main cumulative evidence indicates that short-term aerobic exercise, based on several aerobic intervention formats, seems to be effective for mitigating symptoms such as attention, hyperactivity, impulsivity, anxiety, executive function and social disorders in children with ADHD.

.....

Child Health Care. 2015;44:169-82.

CORRELATES AND MEDIATORS OF LIFE SATISFACTION AMONG YOUTH WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.

Nadeau JM, Jacob ML, Keene AC, et al.

The current study examined factors associated with life satisfaction among 111 youth, ages 8-17 years, presenting for outpatient treatment of attention-deficit/hyperactivity disorder (ADHD). Youth completed the Students Life Satisfaction Scale, Vanderbilt ADHD Diagnostic Rating Scale-Child, and the Generalized Anxiety Disorder (GAD) and Major Depressive Disorder (MDD) modules of the Revised Childs Anxiety and Depression Scale. A primary caregiver completed a standard demographic form, and the Vanderbilt ADHD Diagnostic Rating Scale-Parent. Results indicated that child-rated ADHD symptoms, depressive symptoms, and generalized anxiety symptoms were negatively related to life satisfaction. Parent-rated ADHD symptoms in the child were related to child-rated ADHD symptoms but not to depressive symptoms, generalized anxiety symptoms, or life satisfaction. Depressive symptoms predicted life satisfaction above and beyond parent-rated ADHD symptom severity; however, neither depressive nor generalized anxiety symptoms mediated the relationship between child-rated ADHD symptom severity and life satisfaction. Assessment and treatment implications are discussed; specifically, we highlight how the variables of interest may impact clinical presentation and treatment course.

.....

Childs Nerv Syst. 2015 May.

STREPTOCOCCAL INFECTION AND IMMUNE RESPONSE IN CHILDREN WITH TOURETTE'S SYNDROME.

Li E, Ruan Y, Chen Q, et al.

BACKGROUND: Streptococcal infection and basal ganglia inflammation are hypothesized to be involved in Tourette's syndrome (TS). There is a need for effective therapies for managing TS. We studied streptococcal infection and immunity in TS following immunomodulator (pidotimod) therapy.

METHODS: Blood samples from 58 patients with TS and 128 age-matched healthy controls enabled measurement of antistreptolysin O (ASO), T cells, natural killer (NK) cells, interleukin-6 (IL-6) and interleukin-8 (IL-8), and tumor necrosis factor-alpha (TNF-alpha). Forty-four patients with abnormal T cell numbers were divided into two groups and treated with pidotimod granules (pidotimod group, n = 20) or pidotimod plus dopaminergic receptor antagonists (combination group, n = 24). Yale Global Tic Severity Scale (YGTSS) scores and immunologic indices were assessed after treatment.

RESULTS: An ASO >1:200 was found in 22.4 % of children with TS, 7.5 % of controls, and 38.9 % of children with both TS and attention deficit hyperactivity disorder (ADHD) compared to 15.0 % of children with TS alone (P < 0.05). Children with TS showed decreased CD3+ and CD4+ T cells, CD4+/CD8+ ratio, IL-6 and IL-8, increased NKC and TNF-alpha (P < 0.05) as compared to controls. ASO-positive children with TS had lower CD4+ T cells as compared to ASO-negative children with TS, and lower IL-6 and IL-8 levels as compared to controls (P < 0.05). After 8 weeks of pidotimod treatment, IL-8 was increased compared to either tiapride hydrochloride or haloperidol and pidotimod (P < 0.05).

CONCLUSIONS: Streptococcal infection in TS patients is associated with immune and cytokine dysfunction, which can be potentially managed with immunomodulator therapy.

Chin J Evid -Based Med. 2015;15:403-08.

CLINICAL PRACTICE GUIDELINES ON ATTENTION-DEFICIT/HYPERACTIVITY DISORDER IN CHILDREN AND ADOLESCENTS: A SYSTEMATIC REVIEW.

Liu M-B, Zheng B, Li N, et al.

Objective To systematically review the methodological quality of guidelines concerning attentiondeficit/ hyperactivity disorder (ADHD) in children and adolescents, and to compare differences and similarities of the drugs recommended, in order to provide guidance for clinical practice.

Methods Guidelines concerning ADHD were electronically retrieved in PubMed, EMbase, VIP, WanFang Data, CNKI, NGC (National Guideline Clearinghouse), GIN (Guidelines International Network), NICE (National Institute for Health and Clinical Excellence) from inception to December 2013. The methodological quality of included guidelines were evaluated according to the AGREE II instrument, and the differences between recommendations were compared.

Results A total of 9 guidelines concerning ADHD in children and adolescents were included, with development time ranging from 2004 to 2012. Among 9 guidelines, 4 were made by the USA, 3 in Europe and 2 by UK. The levels of recommendations were Level A for 2 guidelines, and Level B for 7 guidelines. The scores of guidelines according to the domains of AGREE II decreased from nullclarity of presentationsnull, nullscope and purposenull, nullparticipantsnull, nullapplicabilitynull, nullrigour of developmentnull and nulleditorial independencenull. Three evidence-based guidelines scored the top three in the domain of nullrigour of developmentnull. There were slightly differences in the recommendations of different guidelines.

Conclusion The overall methodological quality of ADHD guidelines is suboptimal in different countries or regions. The 6 domains involving 23 items in AGREE II vary with scores, while the scores of evidence-base guidelines are higher than those of non-evidence-based guidelines. The guidelines on ADHD in children and adolescents should be improved in nullrigour of developmentnull and nullapplicabilitynull in future. Conflicts of interest should be addressed. And the guidelines are recommended to be developed on the basis of methods of evidence-based medicine, and best evidence is recommended.

.....

Clin Toxicol (Phila). 2015 May;53:210-14.

DIFFERENCES IN ABUSE POTENTIAL OF ADHD DRUGS MEASURED BY CONTRASTING POISON CENTRE AND THERAPEUTIC USE DATA.

Jensen LS, Pagsberg AK, Dalhoff KP.

CONTEXT: Atomoxetine (ATX) is the treatment of choice for attention deficit hyperactivity disorders with co-morbid risk of drug abuse, although its abuse potential needs to be qualified. The purpose of this study is to analyse ATX misuse in relation to therapeutic use and compare our results with that of methylphenidate (MPH).

METHODS AND MATERIALS: Data on enquiries were extracted from the Danish Poison Information Centre database (January 2006 to June 2012), while data on therapeutic use were provided by the Danish State Serum Institute (2007-2011).

RESULTS: The study included 28 ATX and 394 MPH enquiries. Frequency of ATX enquiries did not show a significant correlation to either sale or number of treated patients but for MPH, both correlations were significant (p = 0.001 and p = 0.0008, respectively). The enquiries/number of treated patients relationship differed significantly between ATX and MPH (p = 0.018), but not the enquiries/sale relationship. The proportion of exposures motivated by recreational drug use was significantly lower for ATX (19%) than that for MPH (40%) (p = 0.038).

DISCUSSION AND CONCLUSION: These results suggest that ATX is used by adults for non-medical purposes including recreational use, but to a lesser extent than MPH.

Clin Exp Allergy. 2015;45:964-73.

IMPACT OF ASTHMA MEDICATION AND FAMILIAL FACTORS ON THE ASSOCIATION BETWEEN CHILDHOOD ASTHMA AND ATTENTION-DEFICIT/HYPERACTIVITY DISORDER: A COMBINED TWIN- AND REGISTER-BASED STUDY.

Holmberg K, Lundholm C, Anckarsater H, et al.

Background: Asthma and attention-deficit/hyperactivity disorder (ADHD) are prevalent in childhood and may cause functional impairment and stress in families. Previous research supports an association between asthma and ADHD in children, but several aspects of this relationship are unclear.

Objective: Our aim was to study whether the association between asthma and ADHD is restricted to either the inattentive or the hyperactive/impulsive symptoms of ADHD, to explore the impact of asthma severity and asthma medication and the contribution of shared genetic and environmental risk factors on the asthma-ADHD relationship.

Methods: Data on asthma, ADHD, zygosity and possible confounders were collected from parental questionnaires at 9 or 12 years on 20 072 twins through the Swedish Twin Register, linked to the Swedish Medical Birth Register, the National Patient Register and the Prescribed Drug Register. The association between asthma and ADHD, the impact of asthma severity and medication, was assessed by generalized estimating equations. Cross-twin-cross-trait correlations (CTCT) were estimated to explore the relative importance of genes and environment for the association.

Results: Asthmatic children had a higher risk of also having ADHD [odds ratio (OR) 1.53, 95% confidence interval (CI): 1.16-2.02]. The association was not restricted to either of the two dimensions of ADHD. The magnitude of the association increased with asthma severity (OR 2.84, 95% CI: 1.86-4.35) for (greater-than or equal to) 4 asthma attacks in the last 12 months and was not affected by asthma treatment. The CTCTs possibly indicate that the genetic component in overlap of the disorders is weak.

Conclusions and Clinical Relevance: Childhood asthma, especially severe asthma, is associated with ADHD. Asthma medication seems not to increase the risk of ADHD. Clinicians should be aware of the potential of ADHD in asthma. Optimal asthma care needs to be integrated with effective evaluation and treatment of ADHD in children with co-existing disorders.

.....

Clin EEG Neurosci. 2015;46:88-93.

ELECTROENCEPHALOGRAPHIC ACTIVITY BEFORE AND AFTER COGNITIVE EFFORT IN CHILDREN WITH ATTENTION DEFICIT/HYPERACTIVITY DISORDER.

Buyck I, Wiersema JR.

Numerous studies have detected elevated electroencephalographic (EEG) theta/beta ratio (TBR) or theta power in children with attention deficit/hyperactivity disorder (ADHD) and therefore TBR has been suggested to be a promising biomarker of ADHD. At the same time, recent theoretical models have emphasized the heterogeneity of ADHD and the notion that cognitive deficits in ADHD are not fixed but fluctuate according to contextual and state factors. Surprisingly, so far the context- or state-dependency of EEG abnormalities in ADHD has hardly been addressed. Therefore, in the current study, 3 minutes eyes closed resting EEG before and after execution of 3 n-back tasks were compared between 21 children with ADHD and 22 typically developing children. No difference between groups was found for TBR or theta power (or other frequency bands), neither before nor after task execution, indicating that enhanced TBR or theta power is not to be considered universal for the disorder. Hence, cautiousness is warranted in using these indices for diagnostic purposes in ADHD. Across groups, posterior theta power, as well as central and posterior beta power was attenuated after task execution, which was interpreted as the children experiencing a more alert state after cognitive effort. Yet, this EEG modulation was similar in both groups, providing no support for a context-or state-dependency of EEG abnormalities in ADHD. However, in light of the absence of any group differences in EEG parameters, further research is warranted.

Clin Neuropharmacol. 2015 Mar;38:60-61.

METHYLPHENIDATE-INDUCED AWAKE BRUXISM: A CASE REPORT.

Sivri RÇ, Bilgiç A.

Methylphenidate (MPH) is a stimulant that is commonly used in the treatment of attentiondeficit/hyperactivity disorder in children and adults. Several reports are available regarding the relationship of MPH use and sleep bruxism. We report the case of a 9-year-old boy who presented with severe awake bruxism after his second dose of sustained release form of MPH treatment, which was confirmed on rechallenge. This is the first report of its kind showing such relationship in the literature.

.....

Clin Pract Epidemiol Ment Health. 2014;10:176-83.

A COMPARISON BETWEEN CHILDREN WITH ADHD AND CHILDREN WITH EPILEPSY IN SELF-ESTEEM AND PARENTAL STRESS LEVEL.

Gagliano A, Lamberti M, Siracusano R, et al.

Attention-deficit/hyperactivity disorder (ADHD) is frequently associated with negative psychological outcomes. This study explores the relationship between self-esteem, ADHD symptoms and parental stress. It compares children with ADHD, children with epilepsy (E) and typical developmental controls (TD). Participants included 65 children (aged 9-12 yrs) and their parents. The assessment was conducted by Multidimensional Self-Concept Scale (MSCS), Parent Stress Index (PSI) and Conners' Parent Rating Scales-Revised. Significant differences were found in Social, Competence and Academic areas of self-esteem between children with ADHD, with E and TD. Moreover, parents of children with ADHD showed a higher overall stress than both other groups. In conclusion, it seems important to evaluate the psychological aspects of ADHD condition, both in children and in parents, in order to suggest an individual multimodal treatment.

.....

Cogn Behav Pract. 2015 May;22:116-26.

COGNITIVE-BEHAVIORAL THERAPY FOR ADHD IN ADOLESCENTS: CLINICAL CONSIDERATIONS AND A CASE SERIES. Sprich SE, Burbridge J, Lerner JA, et al.

Although ADHD in adolescents is an impairing and prevalent condition, with community prevalence estimates between 2% and 6%, psychosocial treatments for adolescents compared to younger children are relatively understudied. Our group has successfully developed an evidence base for cognitive-behavioral therapy (CBT) for ADHD in medication-treated adults with ADHD with clinically significant symptoms. In the current paper, we describe an adaptation of this treatment to adolescents, and provide case reports on 3 adolescents who participated in an open pilot trial. The results suggest that the treatment approach was well tolerated by the adolescents and that they experienced clinical benefit. This early report of the approach in adolescents is promising and requires further efficacy testing.

.....

Cogn Behav Pract. 2015 May;22:141-51.

A COGNITIVE-BEHAVIOR THERAPY AND MENTORING PROGRAM FOR COLLEGE STUDENTS WITH ADHD. Anastopoulos AD, King KA.

College students with ADHD are at increased risk for a number of functional impairments, the severity of which is of sufficient clinical significance to warrant intervention (DuPaul & Weyandt, 2009). Very little treatment research of this type has been conducted to date (Green & Rabiner, 2012). The need for such research is critical, given the increasing numbers of students with ADHD attending college (Pryor, Hurtado, DeAngelo, Blake, & Tran, 2010), their increased risk for dropping out of college, and the known negative life outcomes for which they may be at increased risk later as adults (Barkley, Murphy, & Fischer, 2008). To address this situation we recently developed and began testing Accessing Campus Connections and Empowering Student Success (ACCESS). The active phase of ACCESS provides group cognitive behavior

therapy (CBT), accompanied by individual mentoring. Booster group CBT and mentoring sessions are provided during a maintenance phase. Preliminary findings have revealed significant increases in ADHD knowledge, use of organizational skills, and reductions in maladaptive thinking, all of which are presumed mechanisms of clinical change. Such changes have been accompanied by reductions in ADHD symptoms, improvements in executive functioning, educational benefits, improved emotional well-being, and increased use of disability services and other campus resources. Although promising, such findings are limited by the fact that ACCESS has thus far been tested in an open clinical trial. Thus, additional research is needed to determine its efficacy and effectiveness.

.....

Complement Ther Clin Pract. 2015 May;21:61-67.

GINKGO BILOBA IN THE TREATMENT OF ATTENTION-DEFICIT/HYPERACTIVITY DISORDER IN CHILDREN AND ADOLESCENTS. A RANDOMIZED, PLACEBO-CONTROLLED, TRIAL.

Shakibaei F, Radmanesh M, Salari E, et al.

OBJECTIVE: To evaluate the efficacy of Ginkgo biloba as a complementary therapy for attentiondeficit/hyperactivity disorder (ADHD).

METHODS: Children and adolescents with ADHD received methylphenidate (20-30 mg/day) plus either G. biloba (80-120 mg/day) or placebo for 6 weeks. Parent and teacher forms of the ADHD Rating Scale-IV (ADHD-RS-IV) were completed at baseline, week 2, and week 6. Treatment response was defined as 27% improvement from baseline in the ADHD-RS-IV.

RESULTS: Compared with placebo, more reduction was observed with G. biloba regarding ADHD-RS-IV parent rating inattention score (-7.74 +/- 1.94 vs. -5.34 +/- 1.85, P < 0.001) and total score (-13.1 +/- 3.36 vs. -10.2 +/- 3.01, P = 0.001) as well as teacher rating inattention score (-7.29 +/- 1.90 vs. -5.96 +/- 1.52, P = 0.004). Response rate was higher with G. biloba compared with placebo based on parent rating (93.5% vs. 58.6%, P = 0.002).

CONCLUSIONS: The G. biloba is an effective complementary treatment for ADHD. Further studies with longer treatment duration are warranted in this regard. IRCT2014111519958N1

.....

Croat Med J. 2015;56:159-65.

PREVALENCE AND INCIDENCE OF ATTENTION-DEFICIT/HYPERACTIVITY DISORDER IN SLOVENIAN CHILDREN AND ADOLESCENTS: A DATABASE STUDY FROM A NATIONAL PERSPECTIVE.

Stuhec M, Svab V, Locatelli I.

Aim: To estimate prevalence and incidence of attention deficit hyperactivity disorder (ADHD) in children and adolescents in Slovenia using different epidemiological models.

Methods: Data from the National Institute of Public Health of the Republic of Slovenia for the period 1997-2012 were analyzed. The database includes the annual number of newly diagnosed outpatients with ADHD in Slovenia. The evaluation for ADHD diagnoses was done in accordance with the Tenth Revision of the International Classification of Diseases (ICD-10) outpatient data codes. In model 1, a linear increase was proposed to fit the data in the period from 1997 to 2003 in order to extrapolate the data before 1997. In model 2 and 3, an exponential increase in the annual incidence rate was proposed.

Results: The incidence rate of ADHD diagnosis in 1997 was 0.032% and in 2012 it increased to 0.082%. Mean prevalence rate was 750 (95% confidence interval: 660-840) per 100 000 children and adolescents. It was estimated that the prevalence rate in 2020 would be 1% (95% confidence interval: 0.875-1.125), which is 6.3-fold higher than in 1997.

Conclusions: ADHD is a common mental health disorder among Slovenian children and adolescents, but it remained underdiagnosed compared with Western countries. Our results indicated a need for improved timely interventions in Slovenia, not only in child and adolescent psychiatry but also in primary settings and adult psychiatry, where ADHD should be more efficiently recognized.

Curr Psychiatry Rep. 2015;17.

SPECIFIC LEARNING DISORDERS AND ADHD: CURRENT ISSUES IN DIAGNOSIS ACROSS CLINICAL AND EDUCATIONAL SETTINGS.

Pham AV, Riviere A.

With the recent changes in the American Psychiatric Associationnulls Diagnostic and Statistical Manual of Mental Disorders (DSM), this article provides a comprehensive review of two high-incidence disorders most commonly seen in childhood and adolescence: specific learning disorder (SLD) and attention-deficit/hyperactivity disorder (ADHD). Updates regarding comorbidity, shared neuropsychological factors, and reasons for the changes in diagnostic criteria are addressed. Although the revisions in the DSM-5 may allow for better diagnostic sensitivity based on the symptomology, specifiers, and the clinical features outlined, there continues to be challenges in operationalizing SLD and implementing consistent assessment practices among mental health professionals particularly when considering the Individuals with Disabilities Education Act (IDEA), which provides guidelines in the evaluation of SLD in school settings. Clinical and educational assessment implications are discussed with special attention to develop a collaborative approach between psychiatrists, psychologists, and educators when providing service delivery for children and adolescents with neurodevelopmental disabilities.

.....

Developmental Science. 2015 May;18:484-94.

INSTITUTIONAL CARE AND IRON DEFICIENCY INCREASE ADHD SYMPTOMOLOGY AND LOWER IQ 2.5-5 YEARS POST-ADOPTION.

Doom JR, Georgieff MK, Gunnar MR.

Increased ADHD symptomology and lower IQ have been reported in internationally adopted (IA) children compared to non-adopted peers (Hostinar, Stellern, Schaefer, Carlson & Gunnar, 2012; Kreppner, O'Connor & Rutter, 2001). However, it is unclear whether these outcomes are due to institutional deprivation specifically or to co-occurring micronutrient deficiencies that disrupt brain development (Fuglestad, Rao & Georgieff, 2008b). In this study, IA children were compared to children raised in their biological families to examine differences in ADHD symptomology and IQ 2.5-5 years post-adoption and to assess the contributions of iron deficiency (ID) and duration of deprivation to these cognitive outcomes. ADHD symptoms (parent- and experimenter-reported) and IQ were evaluated in 88 IA (M = 62.1 months. SD = 2.4) and 35 non-adopted children (M = 61.4 months, SD = 1.6). IA children were assessed 29-64 months post-adoption (M = 41.9 months, SD = 10.2). ID was assessed during the initial post-adoption medical visit in 69 children, and children were classified into four groups by iron status, ranging from normal to ID anemia (most severe). IA children had greater ADHD symptomology, p < .01, and lower IQ, p = .001, than non-adopted children. Within the IA group, children with more severe ID at adoption had greater ADHD symptomology, r(69) = 0.40, p = .001, and lower IQ, r(68) = -0.28, p < .05. Duration of institutional care was positively correlated with ADHD symptoms, r(86) = .28, p < .01, but not IQ, r(85) = -.08, p = .52. Longitudinal results indicate improvement in IQ from 12 months post-adoption to age 5 for children with greater ID severity at adoption and longer duration of institutional care but no improvement in ADHD symptoms. These results signify continuing effects of early deprivation and ID on ADHD symptoms and IQ of vears after adoption. А video abstract this article can be viewed at http://www.youtube.com/watch?v=vUFDAS3DD1c

.....

Environ Health. 2015 May;14:44.

ASSOCIATION OF PYRETHROID PESTICIDE EXPOSURE WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER IN A NATIONALLY REPRESENTATIVE SAMPLE OF U.S. CHILDREN.

Wagner-Schuman M, Richardson JR, Auinger P, et al.

BACKGROUND: Pyrethroid pesticides cause abnormalities in the dopamine system and produce an ADHD phenotype in animal models, with effects accentuated in males versus females. However, data regarding behavioral effects of pyrethroid exposure in children is limited. We examined the association

between pyrethroid pesticide exposure and ADHD in a nationally representative sample of US children, and tested whether this association differs by sex.

METHODS: Data are from 8-15 year old participants (N = 687) in the 2001-2002 National Health and Nutrition Examination Survey. Exposure was assessed using concurrent urinary levels of the pyrethroid metabolite 3-phenoxybenzoic acid (3-PBA). ADHD was defined by either meeting Diagnostic and Statistical Manual of Mental Disorders-Fourth Edition criteria on the Diagnostic Interview Schedule for Children (DISC) or caregiver report of a prior diagnosis. ADHD symptom counts were determined via the DISC. Multivariable logistic regression examined the link between pyrethroid exposure and ADHD, and poisson regression investigated the link between exposure and ADHD symptom counts.

RESULTS: Children with urinary 3-PBA above the limit of detection (LOD) were twice as likely to have ADHD compared with those below the LOD (adjusted odds ratio [aOR] 2.42; 95 % confidence interval [CI] 1.06, 5.57). Hyperactive-impulsive symptoms increased by 50 % for every 10-fold increase in 3-PBA levels (adjusted count ratio 1.50; 95 % CI 1.03, 2.19); effects on inattention were not significant. We observed possible sex-specific effects: pyrethroid biomarkers were associated with increased odds of an ADHD diagnosis and number of ADHD symptoms for boys but not girls.

CONCLUSIONS: We found an association between increasing pyrethroid pesticide exposure and ADHD which may be stronger for hyperactive-impulsive symptoms compared to inattention and in boys compared to girls. Given the growing use of pyrethroid pesticides, these results may be of considerable public health import.

.....

Epilepsia. 2015 May.

SPEED AND COMPLEXITY CHARACTERIZE ATTENTION PROBLEMS IN CHILDREN WITH LOCALIZATION-RELATED EPILEPSY.

Berl MM, Terwilliger V, Scheller A, et al.

OBJECTIVE: Children with epilepsy (EPI) have a higher rate of attention-deficit/hyperactivity disorder (ADHD; 28-70%) than typically developing (TD) children (5-10%); however, attention is multidimensional. Thus, we aimed to characterize the profile of attention difficulties in children with epilepsy.

METHODS: Seventy-five children with localization-related epilepsy ages 6-16 years and 75 age-matched controls were evaluated using multimodal, multidimensional measures of attention including direct performance and parent ratings of attention as well as intelligence testing. We assessed group differences across attention measures, determined if parent rating predicted performance on attention measures, and examined if epilepsy characteristics were associated with attention skills.

RESULTS: The EPI group performed worse than the TD group on timed and complex attention aspects of attention (p < 0.05), whereas performance on simple visual and simple auditory attention tasks was comparable. Children with EPI were 12 times as likely as TD children to have clinically elevated symptoms of inattention as rated by parents, but ratings were a weak predictor of attention performance. Earlier age of onset was associated with slower motor speed (p < 0.01), but no other epilepsy-related clinical characteristics were associated with attention skills.

SIGNIFICANCE: This study clarifies the nature of the attention problems in pediatric epilepsy, which may be under-recognized. Children with EPI had difficulty with complex attention and rapid response, not simple attention. As such, they may not exhibit difficulty until later in primary school when demands increase. Parent report with standard ADHD screening tools may under-detect these higher-order attention difficulties. Thus, monitoring through direct neuropsychological performance is recommended.

Epilepsy Behav. 2015.

METHYLPHENIDATE IMPROVES THE QUALITY OF LIFE OF CHILDREN AND ADOLESCENTS WITH ADHD AND DIFFICULT-TO-TREAT EPILEPSIES.

Radziuk AL, Kieling RR, Santos K, et al.

Objective: Comorbidity between difficult-to-treat epilepsies and ADHD is frequent and impacts negatively on quality of life. The commonly held (yet poorly substantiated) view that stimulants may worsen seizure control has prevented studies from evaluating the impact of such treatment in this population. Our aim was to study the effect of methylphenidate on the quality of life of children and adolescents with difficult-to-treat epilepsies and comorbid ADHD.

Methods: The study was an open-label, noncontrolled trial with intention-to-treat analysis following 30 patients for 6. months. Subjects received methylphenidate following 3. months of baseline, during which antiepileptic drugs (AEDs) were adjusted and epilepsy, ADHD, and quality-of-life variables were assessed. Multivariate regression analysis identified the main variables correlated with outcome.

Results: Only one patient withdrew because of seizure worsening. Following methylphenidate introduction, doses were titrated up to 0.40-0.50. mg/kg/day. A marked improvement in quality-of-life scores and a significant reduction in seizure frequency and severity were observed. Female sex, reduction of core ADHD symptoms, and tolerability to adequate doses of methylphenidate were significantly associated with improved quality-of-life scores.

Conclusion: These preliminary data suggest that methylphenidate treatment is safe and effective in patients with ADHD and difficult-to-treat epilepsies, positively impacting on quality-of-life scores.

.....

Eur Child Adolesc Psychiatry. 2015 May;24:545-52.

PREDICTORS OF AND BARRIERS TO SERVICE USE FOR CHILDREN AT RISK OF ADHD: LONGITUDINAL STUDY. Sayal K, Mills J, White K, et al.

Many children with, or at risk of, ADHD do not receive healthcare services for their difficulties. This longitudinal study investigates barriers to and predictors of specialist health service use. This is a 5-year follow-up study of children who participated in a cluster randomised controlled trial, which investigated school-level interventions (provision of books with evidence-based information and/or feedback of names of children) for children at risk of ADHD. 162 children who had high levels of ADHD symptoms at age 5 (baseline) were followed up at age 10 years. Using baseline data and follow-up information collected from parents and teachers, children who had and had not used specialist health services over the follow-up period were compared and predictors (symptom severity, comorbid problems, parental perception of burden, parental mental health, and socio-demographic factors) of specialist service use investigated. The most common parent-reported barrier reflected lack of information about who could help. Amongst children using specialist health services who met criteria for ADHD at follow-up, 36 % had been prescribed stimulant medication. Specialist health service use was associated with each one-point increase in teacherrated symptoms at baseline [inattention symptoms (adjusted OR = 1.40; 95 % CI 1.12-1.76) and hyperactivity/impulsivity symptoms (adjusted OR = 1.23; 95 % CI 1.05-1.44)]. Parental mental health problems were also independently associated with service use (for each one-point increase in symptoms, adjusted OR = 1.41; 95 % CI 1.04-1.91). Severity of teacher-rated ADHD symptoms in early school years is a determinant of subsequent service use. Clinicians and teachers should be aware that parental mental health problems are independently associated with service use for children at risk of ADHD.

Eur Child Adolesc Psychiatry. 2015 May.

FUNCTIONAL OUTCOMES FROM A HEAD-TO-HEAD, RANDOMIZED, DOUBLE-BLIND TRIAL OF LISDEXAMFETAMINE DIMESYLATE AND ATOMOXETINE IN CHILDREN AND ADOLESCENTS WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER AND AN INADEQUATE RESPONSE TO METHYLPHENIDATE.

Nagy P, Hage A, Coghill DR, et al.

Attention-deficit/hyperactivity disorder (ADHD) is associated with functional impairments in multiple domains of patients' lives. A secondary objective of this randomized, active-controlled, head-to-head, double-blind, dose-optimized clinical trial was to compare the effects of lisdexamfetamine dimesylate (LDX) and atomoxetine (ATX) on functional impairment in children and adolescents with ADHD. Patients aged 6-17 years with an ADHD Rating Scale IV total score >/=28 and an inadequate response to methylphenidate treatment (judged by investigators) were randomized (1:1) to once-daily LDX or ATX for 9 weeks. Parents/guardians completed the Weiss Functional Impairment Rating Scale-Parent Report (WFIRS-P) at baseline and at week 9 or early termination. p values were nominal and not corrected for multiple comparisons. Of 267 randomized patients, 200 completed the study (LDX 99, ATX 101). At baseline, mean WFIRS-P total score in the LDX group was 0.95 [standard deviation (SD) 0.474; 95 % confidence interval (CI) 0.87, 1.03] and in the ATX group was 0.91 (0.513; 0.82, 1.00). Scores in all WFIRS-P domains improved from baseline to endpoint in both groups, with least-squares mean changes in total score of -0.35 (95 % CI -0.42, -0.29) for LDX and -0.27 (-0.33, -0.20) for ATX. The difference between LDX and ATX was statistically significant (p < 0.05) for the Learning and School (effect size of LDX vs ATX, 0.43) and Social Activities (0.34) domains and for total score (0.27). Both treatments reduced functional impairment in children and adolescents with ADHD; LDX was statistically significantly more effective than ATX in two of six domains and in total score.

.....

Eur J Clin Pharmacol. 2015 May.

THE USE OF MELATONIN IN SWEDISH CHILDREN AND ADOLESCENTS-A REGISTER-BASED STUDY ACCORDING TO AGE, GENDER, AND MEDICATION OF ADHD.

Furster C, Hallerback MU.

PURPOSE: The use of melatonin is increasing among Swedish children and adolescents despite deficient knowledge of usage in these groups. The aim of this study was to investigate the use of melatonin in Swedish children and adolescents according to age, gender, dosage, treatment duration, and use of attention deficit hyperactivity disorder (ADHD) medication.

METHODS: Data from the Swedish Prescribed Drug Register was analyzed for children and adolescents 0-19 years old in Sweden during 2006-2013.

RESULTS: The number of new users of melatonin in 2013 was 4296 and 3093 among boys and girls, respectively. Girls started treatment with melatonin in older ages compared to boys. Regular users of melatonin were most common among boys 10-14 years. The average defined daily dose (DDD) per regular user was decreasing from 2.4 DDD in 2006 to 1.7 DDD in 2012. Among girls and boys 5-9 years who were regular users in 2010, over 40 and 50 %, respectively, were still regular users in 2013. In the age group 15-19 years, only about 10 % were still regular users in 2013. In 2013, 65 % of boys and 49 % of girls, using melatonin regularly, also used medication for ADHD regularly.

CONCLUSIONS: More Swedish boys than girls used melatonin regularly. The boys started treatment earlier and more often combined regular use of melatonin with regular use of medication for ADHD. This indicates that girls and boys partly are prescribed melatonin for different reasons. About half of the younger children stayed on melatonin treatment for several years, while 90 % of adolescents (15-19 years) concluded their treatment.

Eur Child Adolesc Psychiatry. 2015;24:575-90.

PREVALENCE AND DIAGNOSTIC VALIDITY OF MOTIVATIONAL IMPAIRMENTS AND DEFICITS IN VISUOSPATIAL SHORT-TERM MEMORY AND WORKING MEMORY IN ADHD SUBTYPES.

Dovis S, Van der Oord S, Huizenga HM, et al.

Deficits in working memory (WM) and reinforcement sensitivity are thought to give rise to symptoms in the combined (ADHD-C) and inattentive subtype (ADHD-I) of ADHD. Children with ADHD are especially impaired on visuospatial WM, which is composed of short-term memory (STM) and a central executive. Although deficits in visuospatial WM and reinforcement sensitivity appear characteristic of children with ADHD on a group-level, the prevalence and diagnostic validity of these impairments is still largely unknown. Moreover, studies investigating this did not control for the interaction between motivational impairments and cognitive performance in children with ADHD, and did not differentiate between ADHD subtypes. Visuospatial WM and STM tasks were administered in a standard (feedback-only) and a highreinforcement (feedback + 10 euros) condition, to 86 children with ADHD-C, 27 children with ADHD-I (restrictive subtype), and 62 typically developing controls (aged 8null12). Reinforcement sensitivity was indexed as the difference in performance between the reinforcement conditions. WM and STM impairments were most prevalent in ADHD-C. In ADHD-I, only WM impairments, not STM impairments, were more prevalent than in controls. Motivational impairments were not common (22 % impaired) and equally prevalent in both subtypes. Memory and motivation were found to represent independent neuropsychological domains. Impairment on WM, STM, and/or motivation was associated with more inattention symptoms, medication-use, and lower IQ scores. Similar results were found for analyses of diagnostic validity. The majority of children with ADHD-C is impaired on visuospatial WM. In ADHD-I, STM impairments are not more common than in controls. Within both ADHD subtypes only a minority has an abnormal sensitivity to reinforcement.

Eur J Paediatr Neurol. 2015.

DIAGNOSTIC OVERSHADOWING IN A POPULATION OF CHILDREN WITH NEUROLOGICAL DISABILITIES: A CROSS SECTIONAL DESCRIPTIVE STUDY ON ACQUIRED ADHD.

.....

Hendriksen JGM, Peijnenborgh JCAW, Aldenkamp AP, et al.

Aim: Diagnostic overshadowing refers to the underdiagnosis of comorbid conditions in children with known neurological diagnoses. To demonstrate diagnostic overshadowing we determined the prevalence of attention deficit-hyperactivity disorders (ADHD) in a cohort of children with a wide range of neurological disabilities.

Method: The study cohort consisted of 685 children (mean age 10.3 years, SD: 3.1; 425 boys and 260 girls) who visited a tertiary outpatient multidisciplinary clinic for neurological learning disabilities. Patients with ADHD were identified by retrospective chart review using DSM-IV criteria.

Results: The prevalence of ADHD in this cohort was 38.8% (266 children); of these children only 28.2% (75 children) were diagnosed with ADHD before referral.

Interpretation: ADHD is a common problem in children with neurological disabilities and may be underdiagnosed due to overshadowing of somatic, physical or syndromal features of the disability. In our heterogeneous population ADHD was overshadowed in 71.8% of the cases. This finding may have important implications for diagnosis and treatment of mental health needs in children with neurological disabilities.

.....

Eur Neuropsychopharmacol. 2015.

GREY MATTER VOLUMES IN TREATMENT NAIVE VS. CHRONICALLY TREATED CHILDREN WITH ATTENTION DEFICIT/HYPERACTIVITY DISORDER: A COMBINED APPROACH.

Villemonteix T, De Brito SA, Kavec M, et al.

Psychostimulants are the first-line treatment in attention deficit/hyperactivity disorder (ADHD), but their effects on brain development remain poorly understood. In particular, previous structural magnetic

resonance imaging (sMRI) studies only investigated treatment effects on grey matter (GM) volumes in selected regions of interest (ROIs). In this study, voxel-based morphometry (VBM) was used to assess medication-related GM volume differences across the entire brain. Automated tracing measurements of selected ROIs were also obtained. Three groups (77 participants aged 7-to-13 year old) underwent MRI scans and were compared: never-medicated children with ADHD (n=33), medicated (methylphenidate) children with ADHD (n=20) and typically developing children (TD: n=24). Optimised VBM was used to investigate regional GM volumes, controlling for age and gender. Automated tracing procedures were also used to assess the average volume of the caudate nucleus, the amygdala and the nucleus accumbens. When compared to both medicated children with ADHD and TD children, never-medicated children with ADHD exhibited decreased GM volume in the insula and in the middle temporal gyrus. When compared to TD children, medicated children with ADHD had decreased GM volume in the middle frontal gyrus and in the precentral gyrus. Finally, ROI analyses revealed a significant association between duration of treatment and GM volume of the left nucleus accumbens in medicated children with ADHD. In conclusion, this study documents potential methylphenidate-related GM volume normalization and deviation in previously unexplored brain structures, and reports a positive association between treatment history and GM volume in the nucleus accumbens, a key region for reward-processing.

.....

Expert Rev Neurother. 2015 Jun;15:711-17.

MELATONIN FOR SLEEP DISTURBANCE IN CHILDREN WITH NEURODEVELOPMENTAL DISORDERS: PROSPECTIVE OBSERVATIONAL NATURALISTIC STUDY.

Ayyash HF, Preece P, Morton R, et al.

BACKGROUND: Although melatonin is increasingly used for sleep disturbances in children with neurodevelopmental disorders, evidence on effective dose and impact on specific types of sleep disturbance is limited.

METHOD: We assessed 45 children (35 males, mean age: 6.3 + - 1.7 years) with neurodevelopmental disorders (n = 29: intellectual disability; n = 9: autism spectrum disorder; n = 7: attention-deficit/hyperactivity disorder) and sleep disturbances, treated with melatonin (mean duration: 326 days) with doses increased according to response.

RESULTS: Thirty-eight percent of children responded to low (2.5-3 mg), 31% to medium (5-6 mg) and 9% to high doses (9-10 mg) of melatonin, with a significant increase in total hours of sleep/night, decreased sleep onset delay and decreased number of awakenings/night (all: p = 0.001), as measured with sleep diaries. No serious adverse events were reported.

CONCLUSIONS: Melatonin is generally effective and safe in children with neurodevelopmental conditions. Increasing above 6 mg/night adds further benefit only in a small percentage of children.

.....

FASEB J. 2015;29.

LOW SERUM SPHINGOLIPIDS IN ATTENTION DEFICIT HYPERACTIVITY DISORDER (ADHD).

Henriquez-Henriquez M, Solari S, Allende F, et al.

Background: ADHD is the most prevalent neurodevelopmental disorder in children and has been associated with a lag in neuronal maturation. Sphingolipids are essential for myelination, neuronal function and development. We hypothesized that serum sphingolipid profiles are different in ADHD.

Objective: To characterize the serum sphingolipid profile in ADHD patients and two independent control groups: non-affected relatives and non-affected subjects without family history of ADHD.

Method: Sphingolipid profiles were determined by mass spectrometry in 77 participants (28 ADHD, 28 related controls and 21 unrelated controls). Diagnosis was based on the criteria of Diagnostic and Statistical Manual of Mental Disorders (DSM IV-TR). Groups were compared by parametrical statistics.

Results: All major sphingomyelins (C16:0, C18:0, C18:1 and C24:1), ceramide C24:0 and deoxyceramide C24:1 were significantly decreased in ADHD at relative reductions between 20-30%. In our sample,

decreased serum sphingomyelin levels distinguished ADHD patients with 79% sensitivity, 78% specificity and an estimated negative predictive value of 97%.

Conclusion: Serum sphingomyelin and select ceramides are decreased in ADHD patients. Longitudinal studies are required to evaluate if these findings reflect an ADHD specific pathomechanisms. Low serum sphingomyelins levels are a potential biomarker for ADHD.

.....

Genet Test Mol Biomarkers. 2015 May.

ASSOCIATION BETWEEN BDNF GENE POLYMORPHISMS AND ATTENTION DEFICIT HYPERACTIVITY DISORDER IN KOREAN CHILDREN.

Kwon HJ, Ha M, Jin HJ, et al.

BACKGROUND: Attention deficit hyperactivity disorder (ADHD) is a common childhood neuropsychiatric disorder characterized by behavioral problems such as attention deficit, hyperactivity, and impulsivity. The brain-derived neurotrophic factor (BDNF) is the most abundant neurotrophin in the brain. AIMS: The aim of the present study was to investigate the association between the genotype and alleles for the BDNF gene in Korean children with ADHD.

METHODS: The sample consisted of 180 ADHD children and 159 control children. We diagnosed ADHD according to the DSM-IV. ADHD symptoms were evaluated with Conners' Parent Rating Scales and Dupaul Parent ADHD Rating Scales. Blood samples were taken from the 339 subjects, DNA was extracted from blood lymphocytes, and polymerase chain reaction was performed for BDNF rs6265, rs11030101, rs10835210, rs7103873, and rs2030324 polymorphisms. Alleles and genotype frequencies were compared using the Chi-square test. We compared the allele and genotype frequencies of the BDNF gene polymorphism in the ADHD and control groups.

RESULTS: This study showed that there was a significant correlation among the allele frequencies of the rs11030101 and rs10835210 single nucleotide polymorphisms (SNPs) (odds ratio=0.61, 95% confidence interval=0.39-0.96, p=0.034), but the final conclusions are not definite. Follow-up studies with larger patient or pure subgroups are expected. These results suggest that the BDNF allelic structure may impact ADHD symptoms.

.....

G Ital Ostet Ginecol. 2014;36:571-75.

ASSESSMENT OF ASSOCIATION BETWEEN ATTENTION DEFICIT HYPERACTIVITY DISORDER AND LOW BIRTH WEIGHT. Saeidi R, Sagari M, Javanbakht M.

.....

Heart Rhythm. 2015 May.

STIMULANT THERAPY IN CHILDREN WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER AND CONCOMITANT LONG QT SYNDROME: A SAFE COMBINATION?

Rohatgi RK, Bos JM, Ackerman MJ.

BACKGROUND: Attention deficit hyperactivity disorder (ADHD) is prevalent in about 11% of U.S. children, and as such, ADHD is expected to be present in patients with long QT syndrome (LQTS), a rare, potentially lethal but highly treatable cardiac channelopathy. ADHD-directed stimulant therapy is relatively contraindicated in patients with LQTS due to concern for LQTS-triggered events.

OBJECTIVE: Evaluate the ADHD-directed treatment, outcome, and frequency of LQTS-triggered events in patients with LQTS and concomitant ADHD.

METHODS: A retrospective electronic medical record review of 357 pediatric patients with LQTS evaluated between 1999-2014 was performed to determine the prevalence of concomitant ADHD and the incidence of LQTS-triggered events in patients with LQTS, with or without concomitant ADHD.

RESULTS: Overall, 28(8%) patients were diagnosed with LQTS concomitant ADHD. There were no phenotypic differences between patients with LQTS and ADHD, and LQTS alone. ADHD-directed stimulant

therapy was stopped or advised against in 19(68%) patients at the time of first evaluation or after diagnosis. None of the 15 stimulant-treated patients experienced LQTS-triggered events in a combined 56 person-years of treatment. Perhaps paradoxically, there was a statistically lower LQTS-triggered event rate in the stimulant-treated ADHD group compared to the LQTS alone cohort.

CONCLUSIONS: Among patients with mild to moderate risk LQTS, we found a prevalence of ADHD similar to the general population, which can be treated effectively and safely with stimulant therapy. Physicians should find reassurance in the low adverse event rate, and should weigh potential effects of suboptimal treatment of ADHD, with the theoretical pro-arrhythmic risk from stimulant medications.

.....

Int J Pediatr Otorhinolaryngol. 2015.

EFFECTS OF ADENOIDECTOMY/ADENOTONSILLECTOMY ON ADHD SYMPTOMS AND BEHAVIORAL PROBLEMS IN CHILDREN.

Aksu H, Gunel C, Ozgur BG, et al.

Objectives: In children, the most common reason of upper airway obstruction (UAO) is adenotonsillar hypertrophy. In literature, the adverse effects of UAO and obstructive sleep apnea syndrome on behavior and attention in children have been reported in several articles. However, the methods used for the evaluation of behavioral disorders have not been standardized in those studies. The aim of this study was to investigate the behavioral and attention characteristics of children before and after adenoidectomy/adenotonsillectomy using an internationally valid method.

Methods: A total of 41 patients, between 6 and 11 years of age and having a medical history of UAO for at least one year for which adenotonsillectomy procedure was indicated, were enrolled in the study. The patients were evaluated for signs of attention/behavioral disorders by a child-adolescent psychiatrist and Kiddie-Schedule for Affective Disorders and Schizophrenia for School-Age Children: Present and Lifetime Version (K-SADS-PL) and The Turgay DSM-IV-Based Child and Adolescent Disruptive Behavioral Disorders Screening and Rating Scale (T-DSM-IV-S), before and at the 6th month following the operation.

Results: In the preoperative period, a psychiatric disorder was identified by K-SADS-PL in 41.4% (n = 17) of patients. Of these, 11 patients had attention deficit hyperactivity disorder (ADHD), 6 had enuresis nocturna, and 2 had separation anxiety disorder. Pre- and postoperative mean scores in T-DSM-IV-S parent scale were 31.3. (plus or minus). 8.5 and 20.2. (plus or minus). 10.3, respectively, and this difference was statistically significant (p <. 0.001).

Conclusion: The relationship of UAO and attention/behavioral disorders should be taken into consideration by child-adolescent psychiatrists together with ENT specialists and a multidisciplinary approach is important for the treatment team

.....

J Abnorm Child Psychol. 2015 May.

REINFORCEMENT AND STIMULANT MEDICATION AMELIORATE DEFICIENT RESPONSE INHIBITION IN CHILDREN WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.

Rosch KS, Fosco WD, Pelham WE, Jr., et al.

This study examined the degree to which reinforcement, stimulant medication, and their combination impact response inhibition in children with Attention-Deficit/Hyperactivity Disorder (ADHD). Across three studies, participants with ADHD (n = 111, 25 girls) and typically-developing (TD) controls (n = 33, 6 girls) completed a standard version of the stop signal task (SST) and/or a reinforcement-manipulation SST with performance-contingent points. In two of these studies, these tasks were performed under placebo or 0.3 and 0.6 mg/kg methylphenidate (MPH) conditions. Cross-study comparisons were conducted to test hypotheses regarding the separate and combined effects of reinforcement and methylphenidate on response inhibition among children with ADHD relative to TD controls. Baseline response inhibition was worse among children with ADHD compared to controls. MPH produced dose-related improvements in response inhibition in children with ADHD; compared to non-medicated TD controls, 0.3 mg/kg MPH normalized deficient response inhibition, and 0.6 mg/kg MPH resulted in better inhibition in children with

ADHD. Reinforcement improved response inhibition to a greater extent for children with ADHD than for TD children, normalizing response inhibition. The combination of MPH and reinforcement improved response inhibition among children with ADHD compared to reinforcement alone and MPH alone, also resulting in normalization of response inhibition despite repeated task exposure. Deficient response inhibition commonly observed in children with ADHD is significantly improved with MPH and/or reinforcement, normalizing inhibition relative to TD children tested under standard conditions.

.....

J Abnorm Child Psychol. 2015 May;43:655-67.

A RANDOMIZED TRIAL EXAMINING THE EFFECTS OF AEROBIC PHYSICAL ACTIVITY ON ATTENTION-DEFICIT/HYPERACTIVITY DISORDER SYMPTOMS IN YOUNG CHILDREN.

Hoza B, Smith AL, Shoulberg EK, et al.

The goal of this study was to compare the effects of before school physical activity (PA) and sedentary classroom-based (SC) interventions on the symptoms, behavior, moodiness, and peer functioning of young children (M age = 6.83) at risk for attention-deficit/hyperactivity disorder (ADHD-risk; n = 94) and typically developing children (TD; n = 108). Children were randomly assigned to either PA or SC and participated in the assigned intervention 31 min per day, each school day, over the course of 12 weeks. Parent and teacher ratings of ADHD symptoms (inattention, hyperactivity/impulsivity), oppositional behavior, moodiness, behavior toward peers, and reputation with peers, were used as dependent variables. Primary analyses indicate that the PA intervention was more effective than the SC intervention at reducing inattention and moodiness in the home context. Less conservative follow-up analyses within ADHD status and intervention groups suggest that a PA intervention may reduce impairment associated with ADHD-risk in both home and school domains; interpretive caution is warranted, however, given the liberal approach to these analyses. Unexpectedly, these findings also indicate the potential utility of a before school SC intervention as a tool for managing ADHD symptoms. Inclusion of a no treatment control group in future studies will enable further understanding of PA as an alternative management strategy for ADHD symptoms.

.....

J Abnorm Child Psychol. 2015 May.

STABILITY OF DISRUPTIVE MOOD DYSREGULATION DISORDER SYMPTOMS (IRRITABLE-ANGRY MOOD AND TEMPER OUTBURSTS) THROUGHOUT CHILDHOOD AND ADOLESCENCE IN A GENERAL POPULATION SAMPLE.

Mayes SD, Mathiowetz C, Kokotovich C, et al.

DSM-5 Disruptive Mood Dysregulation Disorder (DMDD) is a controversial new diagnosis. The DSM-5 conceptualizes DMDD as persistent and chronic, but the stability of the two DMDD symptoms (irritableangry mood and temper outbursts) over time is not known. Mothers rated DMDD symptoms in a population-based sample of 376 children (54 % male) evaluated at 6-12 years (M 9) and again an average of 8 years later (M 16). Mean scores on irritable-angry mood plus temper outbursts at baseline and followup were below sometimes a problem, but were higher at baseline than follow-up. Irritable-angry mood and temper outbursts were both often or very often a problem for 9 % of children at baseline, 6 % at follow-up, and 3 % at baseline and follow-up. Only 29 % of children whose baseline symptoms were often or very often continued to have follow-up symptoms at this level (remission rate 71 %). Less than half (45 %) of the children whose symptoms were often or very often at follow-up had these symptoms 8 years earlier (55 % new cases). Our finding of 71 % remission and 55 % new cases indicates instability of DMDD symptoms over an 8-year period. However, the finding that 29 % still had symptoms often or very often 8 years later is clinically significant. DMDD symptoms were found in only one child who did not have symptoms of oppositional defiant disorder (ODD), conduct disorder, ADHD, anxiety, or depression. This suggests that DMDD symptoms are a feature of multiple disorders, particularly ODD, and do not occur in isolation. questioning the validity of DMDD as a unique and independent diagnosis.

27

J Affect Disord. 2015 Jul;179:167-74.

A CASE-CONTROL STUDY OF THE DIFFICULTIES IN DAILY FUNCTIONING EXPERIENCED BY CHILDREN WITH DEPRESSIVE DISORDER.

Usami M, Iwadare Y, Watanabe K, et al.

OBJECTIVE: The parent-assessed children-with-difficulties questionnaire (Questionnaire-Children with Difficulties; QCD) is designed to evaluate a childs difficulties in functioning during specific periods of the day. This study aimed to use the QCD to evaluate the difficulties in daily functioning experienced by children with depressive disorders.

METHODS: A case-control design was used. The cases comprised 90 junior high school students with depressive disorder, whereas a community sample of 363 junior high school students was enrolled as controls. Behaviors were assessed using the QCD, Depression Self-Rating Scale (DSRS), Tokyo Autistic Behavior Scale (TABS), attention deficit hyperactivity disorder-rating scale (ADHD-RS), and Oppositional Defiant Behavior Inventory (ODBI). We then analyzed the effects of sex and diagnosis on the QCD scores as well as the correlation coefficients between the QCD and the other questionnaires.

RESULTS: We included 90 cases (33 boys, 57 girls) with depressive disorders and 363 controls (180 boys, 183 girls). The QCD scores for the children with depressive disorders were significantly lower compared with those from the community sample (P<0.001). The morning, school-time, and night subscores of the QCD were lower for the children with both depressive disorders and truancy problems than for those with depressive disorders alone (P<0.001). Significant correlations were observed between the following: the night QCD subscore and the DSRS scores among boys, the morning QCD subscore and ADHD-RS inattention scores for all groups, and the evening QCD subscore and the TABS score.

CONCLUSIONS: Parents reported that children with depressive disorders experienced greater difficulties in completing basic daily activities compared with community controls. These difficulties were dependent on sex, symptoms, and the time of day. The use of QCD to assess children with depressive disorders enables clinicians to clarify the time periods at which the children face difficulties.

.....

J Am Acad Child Adolesc Psychiatry. 2015 Jun;54:479-86.

EXAMINING AND COMPARING SOCIAL PERCEPTION ABILITIES ACROSS CHILDHOOD-ONSET NEURODEVELOPMENTAL DISORDERS.

Baribeau DA, Doyle-Thomas KA, Dupuis A, et al.

OBJECTIVE: Several neurodevelopmental disorders are associated with social processing deficits. The objective of this study was to compare patterns of social perception abilities across obsessive-compulsive disorder (OCD), attention-deficit/hyperactivity disorder (ADHD), autism spectrum disorder (ASD), and control participants.

METHOD: A total of 265 children completed the Reading the Mind in the Eyes Test-Child Version (RMET). Parents or caregivers completed established trait/symptom scales. The predicted percentage of accuracy on the RMET was compared across disorders and by item difficulty and item valence (i.e., positive/negative/neutral mental states), then analyzed for associations with trait/symptom scores.

RESULTS: The percentage of correct RMET scores varied significantly between diagnostic groups (p < .0001). On pairwise group comparisons controlling for age and sex, children with ADHD and ASD scored lower than the other groups (p < .0001). When IQ was also controlled for in the model, participants with OCD performed better than controls (p < .001), although differences between other groups were less pronounced. Participants with ASD scored lowest on easy items. Those with ASD and ADHD scored significantly lower than other groups on items with positive valence (p < .01). Greater social communication impairment and hyperactivity/impulsivity, but not OCD traits/symptoms, were associated with lower scores on the RMET, irrespective of diagnosis.

CONCLUSION: Social perception abilities in neurodevelopmental disorders exist along a continuum. Children with ASD have the greatest deficits, whereas children with OCD may be hypersensitive to social information. Social communication deficits and hyperactive/impulsive traits are associated with impaired social perception abilities; these findings highlight overlapping cognitive and behavioral manifestations across disorders.

.....

J Atten Disord. 2015 May.

MANAGING ANXIETY IN CHILDREN WITH ADHD USING COGNITIVE-BEHAVIORAL THERAPY: A PILOT RANDOMIZED CONTROLLED TRIAL.

Sciberras E, Mulraney M, Anderson V, et al.

OBJECTIVE: This pilot randomized controlled trial examined the acceptability and feasibility of a cognitivebehavioral therapy (CBT) intervention for children with ADHD and anxiety, and provided preliminary information on child and family outcomes.

METHOD: Children with ADHD and anxiety (8-12 years) were randomized to receive an adapted version of the Cool Kids CBT program or usual clinical care. Key outcomes included feasibility and acceptability of the intervention (participant enrollment, drop-out, intervention session attendance), remission of anxiety assessed via diagnostic interview, ADHD symptom severity, quality of life (QoL), and parent mental health.

RESULTS: Twelve children participated (67% uptake). Most families attended all 10 intervention sessions, with no drop-outs. Intervention participants had marked improvements in both child and family well-being by parent and teacher report, including anxiety, ADHD symptom severity, QoL, and parent mental health.

CONCLUSION: Non-pharmacological interventions may improve important domains of functioning for children with ADHD and anxiety, including ADHD symptom severity

.....

J Atten Disord. 2015 Jun;19:468-75.

How Informative Is the CANTAB to Assess Executive Functioning in Children With ADHD? A Controlled Study.

Fried R, Hirshfeld-Becker D, Petty C, et al.

OBJECTIVE: The authors examined the utility of the computerized Cambridge Neuropsychological Test Automated Battery (CANTAB) to evaluate executive functioning deficits in children with ADHD.

METHOD: Participants were unmedicated children and adolescents with (n = 107) and without (n = 45) Diagnostic and Statistical Manual of Mental Disorders (4th ed.) ADHD. The authors administered the CANTAB Eclipse battery, which comprises specific tasks shown to be deficient in individuals with ADHD.

RESULTS: With the exception of the affective go/no-go total omissions, ADHD participants were significantly more impaired on all other subtests of the CANTAB in comparison with controls. Effect sizes for individual CANTAB tests were largely in the medium range with the largest effect sizes seen in spatial working memory total and between errors.

CONCLUSION: These CANTAB results are highly congruent with those reported in studies using traditional neuropsychological testing batteries, supporting the utility of the CANTAB to assess neuropsychological deficits in children with ADHD in clinical and research settings

.....

J Atten Disord. 2015 Jun;19:515-26.

DIFFERENTIAL EFFECT OF COGNITIVE TRAINING ON EXECUTIVE FUNCTIONS AND READING ABILITIES IN CHILDREN WITH ADHD AND IN CHILDREN WITH ADHD COMORBID WITH READING DIFFICULTIES.

Horowitz-Kraus T.

The comorbidity of ADHD and reading difficulties (ADHD + RD) is believed to be a disability distinct from ADHD alone, with unique challenges faced by individuals suffering from one disability versus the other. We aimed to examine the differential effect of 8 weeks of cognitive training on reading abilities and on

executive functions, through use of the Wisconsin task, in children with ADHD and in children with ADHD + RD. Greater impairments in reading and executive functions, especially in speed of processing, were found in the comorbid group at baseline. The comorbid group showed greater improvements in most measures after training as well. We propose that the cognitive training used in the present study affected not only the immediate abilities of executive functioning but also the secondary ability of reading, especially in the comorbid group, by improving in particular, speed of processing. We suggest that a differential approach should be taken when treating children with ADHD + RD versus treating ADHD children

.....

J Atten Disord. 2015 May.

ADHD IN CHILDHOOD AND/OR ADULTHOOD AS A RISK FACTOR FOR DOMESTIC VIOLENCE OR INTIMATE PARTNER VIOLENCE: A SYSTEMATIC REVIEW.

Buitelaar NJ, Posthumus JA, Buitelaar JK.

OBJECTIVE: To date, treatment programs for adult domestic violence (DV) or intimate partner violence (IPV) have had minimal impact. To make treatment more effective, programs should be adjusted to psychopathology of the offender. As emotional lability and poor emotional self-regulation and self-control are common features of ADHD, it may play a pivotal role as a predictor for adult DV/IPV.

METHOD: This systematic review synthesizes the available evidence for childhood and/or adult ADHD being a risk factor for DV/IPV.

RESULTS: Four case control studies and three cohort studies were included in the review. Although three case control studies showed positive associations between childhood and/or adult ADHD and adult DV/IPV, two did insufficiently control for the presence of comorbid Conduct Disorder (CD) or Antisocial Personality Disorder (ASPD).

CONCLUSION: Cohort studies identified hyperactive, impulsive, and inattention symptoms as risk factors for adult IPV. CD and ASPD were regarded as mediators in three studies.

.....

J Atten Disord. 2015 May.

PHYSICAL FUNCTIONING, EMOTIONAL, AND BEHAVIORAL PROBLEMS IN CHILDREN WITH ADHD AND COMORBID ASD: A CROSS-SECTIONAL STUDY.

Thomas S, Sciberras E, Lycett K, et al.

OBJECTIVE: To examine (a) physical and daily functioning in children with ADHD and autism spectrum disorder (ASD) compared with ADHD alone and (b) whether decreased physical quality of life (QoL) is associated with increased emotional and behavioral problems in children with ADHD-ASD.

METHOD: Cross-sectional study comprising 392 children with confirmed ADHD (ADHD-ASD, n = 93; ADHD alone, n = 299) recruited from 21 pediatric practices in Victoria, Australia. Data were collected via parent and teacher surveys. Key measures included the Strengths and Difficulties Questionnaire (SDQ) and Pediatric Quality of Life Inventory (PedsQL).

RESULTS: Children with ADHD-ASD had poorer QoL across both psychosocial and physical health domains, and also had greater parent-reported behavioral, emotional, and peer problems, compared with children with ADHD alone. Poorer physical QoL partially mediated the relationship between comorbid ASD status and poorer emotional and behavioral functioning.

CONCLUSION: The comorbid overlay of ASD in ADHD appears to influence not only problems in physical functioning but also the severity of problems relating to areas of emotional and behavioral functioning

J Atten Disord. 2015 Jun;19:489-95.

THE CHILDHOOD EXECUTIVE FUNCTION INVENTORY: CONFIRMATORY FACTOR ANALYSES AND CROSS-CULTURAL CLINICAL VALIDITY IN A SAMPLE OF 8- TO 11-YEAR-OLD CHILDREN.

Catale C, Meulemans T, Thorell LB.

OBJECTIVE: The aim was to investigate the psychometric characteristics of the French adaptation of the Childhood Executive Functioning Inventory (CHEXI) in children and to explore the cross-cultural validity of the CHEXI in discriminating between children with ADHD and controls in two culturally different samples (Belgian and Swedish).

METHOD: Study I included normally developing children (n = 242), whereas Study II included both children diagnosed with ADHD (n = 87) and controls (n = 87). CHEXI ratings were collected from parents.

RESULTS: Confirmatory factor analyses replicated the two-factor solution, referred to as inhibition and working memory, which had been identified previously. Both subscales had good psychometric properties. Furthermore, the CHEXI was found to discriminate, with high sensitivity and specificity, between children with ADHD and controls in both cultural samples.

CONCLUSION: The CHEXI can be considered as a valuable screening measure for ADHD in children, but the cross-cultural clinical implications of ratings have to be considered

.....

J Atten Disord. 2015 Jun;19:507-14.

EXECUTIVE FUNCTIONING IN CHILDREN AND ADOLESCENTS WITH SYMPTOMS OF SLUGGISH COGNITIVE TEMPO AND ADHD.

Araujo Jimenez EA, Jane Ballabriga MC, Bonillo MA, et al.

OBJECTIVE: The aim of this study was to observe whether the independent presence of Sluggish Cognitive Tempo (SCT) directly impacts on the Executive Function (EF), and to determine whether there are deficits in EF that are unique to ADHD predominantly inattentive (ADHD-I) or SCT.

METHOD: Seventy-six participants aged 6 to 17 years and their parents were assessed using a diagnostic interview, an instrument that assesses the EF, and another instrument that assesses the SCT. Two hierarchical linear regression models were performed. The first one analyzed the independent relationship between SCT and EF, and the second model added the symptomatology of ADHD-I.

RESULTS: The SCT has a statistically significant direct relation on the EF deficits and remains in the second model even with the inclusion of the ADHD-I.

CONCLUSION: The SCT and ADHD-I symptoms independently promote executive deficits. Children with ADHD-I symptoms showed deficits in most areas of the EF. Deficits in inhibition and initiative are unique to inattention

.....

J Atten Disord. 2015 May.

EXERCISE INTERVENTIONS IN CHILDREN AND ADOLESCENTS WITH ADHD: A SYSTEMATIC REVIEW. *Neudecker C, Mewes N, Reimers AK, et al.*

OBJECTIVE: Exercise has attracted attention as a potential helpful intervention in children with ADHD. Effects are emphasized on cognition, social-emotional, and motor development.

METHOD: A systematic literature search was conducted using the electronic databases Web of Science, PubMed, Scopus, and ERIC to analyze the efficacy of different types of exercise interventions in children and adolescents with ADHD. Seven studies examining the acute and 14 studies examining the long-term effects were included.

RESULTS: The largest effects were reported for mixed exercise programs on ADHD symptomatology and fine motor precision. However, because of the large differences in the study designs, the comparability is limited.

CONCLUSION: At that time, no evidence-based recommendation can be formulated regarding frequency, intensity, or duration of exercise. Nevertheless, some first trends regarding the effects of certain types of

exercise can be identified. When focusing on long-term health benefits in children and adolescents with ADHD, qualitative exercise characteristics might play an important role.

.....

J Atten Disord. 2015 Jun;19:496-506.

A LONGITUDINAL EXAMINATION OF THE DEVELOPMENTAL EXECUTIVE FUNCTION HIERARCHY IN CHILDREN WITH EXTERNALIZING BEHAVIOR PROBLEMS.

Tillman C, Brocki KC, Sorensen L, et al.

OBJECTIVE: Using a 4-year longitudinal design, we evaluated two hypotheses based on developmental executive function (EF) hierarchy accounts in a sample of children with externalizing problems.

METHOD: The participants performed EF tasks when they were between 8 and 12 years (M = 9.93), and again approximately 4 years later when they were between 12 and 15 years (M = 13.36).

RESULTS: Inhibition in middle childhood predicted working memory (WM) 4 years later. Further, deficits in inhibition and sustained attention were more prominent in middle rather than late childhood, whereas poor WM was salient throughout these periods.

CONCLUSIONS: These findings support the hypotheses that EFs develop hierarchically and that EF deficits in ADHD are more prominent in actively developing EFs. They also emphasize ADHD as a developmental disorder.

.....

J Autism Dev Disord. 2015 May;45:1230-37.

VALIDATION OF THE DEVELOPMENTAL, DIMENSIONAL AND DIAGNOSTIC INTERVIEW (3DI) AMONG CHINESE CHILDREN IN A CHILD PSYCHIATRY CLINIC IN HONG KONG.

Lai KY, Leung PW, Mo FY, et al.

Autism spectrum disorder (ASD) is a disorder with high levels of co-morbidities. The Developmental, Dimensional and Diagnostic Interview (3Di) is a relatively new instrument designed to provide dimensional as well as categorical assessment of autistic behaviours among children with normal intelligence. Its sound psychometric properties and relatively short administration time make it a versatile instrument. The 3Di was translated into Chinese (Cantonese) and its applicability among 194 clinic children was examined. Results found excellent reliability and validity, and achieved a sensitivity of 95 % and specificity of 77 %. It was able to capture the diagnosis of ASD among children presenting with attention deficit hyperactivity disorder. However, although the disorder of ASD is considered universal, the use of a western instrument in a Chinese context should also take note of cultural influences that may impact on the manifestation of its symptoms.

.....

J Child Adolesc Psychopharmacol. 2015 May;25:372-75.

NO EVIDENCE FOR PREDICTORS OF RESPONSE TO ATOMOXETINE TREATMENT OF ATTENTION-DEFICIT/HYPERACTIVITY DISORDER SYMPTOMS IN CHILDREN AND ADOLESCENTS WITH AUTISM SPECTRUM DISORDER.

Harfterkamp M, Van Der Meer D, Loo-Neus G, et al.

J Child Adolesc Psychopharmacol. 2015 May;25:323-36.

ABERRANT BEHAVIORS AND CO-OCCURRING CONDITIONS AS PREDICTORS OF PSYCHOTROPIC POLYPHARMACY AMONG CHILDREN WITH AUTISM SPECTRUM DISORDERS.

Logan SL, Carpenter L, Leslie RS, et al.

OBJECTIVES: The purpose of this study was to identify rates and predictors of psychotropic medication polypharmacy among Medicaid-eligible children in South Carolina with autism spectrum disorder (ASD) from 2000 to 2008.

METHODS: Population-based surveillance data were linked with state Medicaid records to obtain a detailed demographic, behavioral, educational, clinical, and diagnostic data set for all Medicaid-eligible 8year-old children (n=629) who were identified and diagnosed with ASD using standardized criteria. Polypharmacy was defined as having interclass psychotropic medication claims overlapping for >/=30 consecutive days at any time during the 2-year study period. Multivariable logistic regression was used to model predictors of any polypharmacy, and for the three most common combinations.

RESULTS: Overall, 60% (n=377) used any psychotropic medication, and 41% (n=153) of those had interclass polypharmacy. Common combinations were attention-deficit/hyperactivity disorder (ADHD) medications with an antidepressant (A/AD), antipsychotic (A/AP) or a mood stabilizer (A/MS). Black children had lower odds of any polypharmacy, as did those eligible for Medicaid because of income or being foster care versus those eligible because of disability. There were no significant associations between polypharmacy and social deficits in ASD for any combination, although children with communication deficits diagnostic of ASD had lower odds of any polypharmacy and A/AP polypharmacy. Children with argumentative, aggressive, hyperactive/impulsive, or self-injurious aberrant behaviors had higher odds of polypharmacy, as did children with diagnosed co-occurring ADHD, anxiety or mood disorders, or conduct/oppositional defiant disorder (ODD) in Medicaid records.

CONCLUSIONS: Future research is warranted to investigate how child-level factors impact combination psychotropic medication prescribing practices and outcomes in ASD

.....

J Child Adolesc Psychopharmacol. 2015 May;25:362-67.

CHANGING PATTERNS OF ALPHA AGONIST MEDICATION USE IN CHILDREN AND ADOLESCENTS 2009-2011.

Fiks AG, Mayne SL, Song L, et al.

OBJECTIVES: The purpose of this study was to describe rates and patterns of long- and short-acting alpha agonist use for behavioral problems in a primary care population following Food and Drug Administration (FDA) approval of the long-acting alpha agonists guanfacine and clonidine.

METHODS: Children and adolescents 4-18 years of age, who received an alpha agonist prescription between 2009 and 2011, were identified from a sample of 45 United States primary care practices in two electronic health record-based research networks. Alpha agonist receipt was identified using National Drug Codes and medication names. The proportion of subjects receiving long- and short-acting prescriptions in each year was calculated and examined with respect to reported mental health diagnoses, and whether indications for use were on-label, had evidence from clinical trials, or had no trial evidence.

RESULTS: In a cohort of 282,875 subjects, 27,671 (10%) received any psychotropic medication and only 4.227 subjects (1.5%) received at least one prescription for an alpha agonist, most commonly a shortacting formulation (83%). Only 20% of alpha agonist use was on-label (use of long-acting formulations for attention-deficit/hyperactivity disorder [ADHD]). Most subjects (68%) received alpha agonists for indications with evidence of efficacy from clinical trials but no FDA approval, primarily short-acting formulations for ADHD and autism; 12% received alpha agonists for diagnoses lacking randomized clinical trial evidence in children, including sleep disorders and anxiety, or for which there was no documented mental health diagnosis. Rates of long-acting alpha agonist use increased more than 20-fold from 0.2% to 4%, whereas rates of short-acting alpha agonist use grew only slightly between 2009 and 2011 from 10.6% to 11.3%.

CONCLUSIONS: Alpha agonist use was uncommon in this population, and most subjects received shortacting forms for conditions that were off-label, but with clinical trial evidence. The safety and efficacy of use for conditions, including sleep disorders and anxiety, lacking evidence from randomized trials, warrant further investigation.

.....

J Child Psychol Psychiatry. 2015 Jun;56:640-47.

CODEVELOPMENT OF ADHD AND EXTERNALIZING BEHAVIOR FROM CHILDHOOD TO ADULTHOOD. *Kuja-Halkola R, Lichtenstein P, D'Onofrio BM, et al.*

BACKGROUND: Attention-Deficit/Hyperactivity Disorder (ADHD) frequently co-occurs with externalizing disorders, but a clear understanding of the etiologic underpinnings is hampered by the limited understanding of the codevelopment of the traits from childhood into early adulthood.

METHODS: Using a birth cohort of 2600 twins, the Swedish Twin study of Child and Adolescent Development study, assessed at ages 8-9, 13-14, 16-17, and 19-20, we investigated the codevelopment of ADHD and externalizing behavior from childhood to adulthood. The analyses examined ADHD-like and externalizing traits, as rated by twins and their parents using the Attention Problems scale and Externalizing scale of the Child Behavior Checklist, and estimated cross-lagged effects (one trait at one time-point predicting the other at the next). The covariation between the traits were decomposed into stable (effects carried over from the prior time-points) and innovative (new effects for each time-point) sources; each source was further decomposed into additive genetics, shared and nonshared environment.

RESULTS: The analysis suggested that externalizing traits in middle childhood (age 8-9) predicted ADHD-like traits in early adolescence (age 13-14), whereas the reverse association was nonsignificant. In contrast, ADHD-like traits in lateadolescence (age 16-17) predicted externalizing traits in early adulthood (age 19-20). The correlation between ADHD-like and externalizing traits increased over time. At all time-points, innovative sources contributed substantially to maintained comorbidity. Genetic effects explained 67% of the covariation at each time-point; importantly, nearly 50% of these effects were innovative.

CONCLUSIONS: This study challenges the belief that ADHD generally precedes externalizing behaviors; rather, change in the etiologic factors across the development is the rule. The effects were due to both new genetic and environmental factors emerging up to young adulthood. Clinicians and researchers needs to consider complex etiologic and developmental models for the comorbidity between ADHD and externalizing behaviors.

.....

J Child Psychol Psychiatry. 2015 May;56:566-76.

WORKING MEMORY AND COGNITIVE FLEXIBILITY-TRAINING FOR CHILDREN WITH AN AUTISM SPECTRUM DISORDER: A RANDOMIZED CONTROLLED TRIAL.

de VM, Prins PJ, Schmand BA, et al.

BACKGROUND: People with autism spectrum disorders (ASDs) experience executive function (EF) deficits. There is an urgent need for effective interventions, but in spite of the increasing research focus on computerized cognitive training, this has not been studied in ASD. Hence, we investigated two EF training conditions in children with ASD.

METHODS: In a randomized controlled trial, children with ASD (n = 121, 8-12 years, IQ > 80) were randomly assigned to an adaptive working memory (WM) training, an adaptive cognitive flexibility-training, or a non-adaptive control training (mock-training). Braingame Brian, a computerized EF-training with gameelements, was used. Outcome measures (pretraining, post-training, and 6-week-follow-up) were neartransfer to trained EFs, far-transfer to other EFs (sustained attention and inhibition), and parent's ratings of daily life EFs, social behavior, attention deficit hyperactivity disorder (ADHD)-behavior, and quality of life.

RESULTS: Attrition-rate was 26%. Children in all conditions who completed the training improved in WM, cognitive flexibility, attention, and on parent's ratings, but not in inhibition. There were no significant differential intervention effects, although children in the WM condition showed a trend toward improvement

on near-transfer WM and ADHD-behavior, and children in the cognitive flexibility condition showed a trend toward improvement on near-transfer flexibility.

CONCLUSION: Although children in the WM condition tended to improve more in WM and ADHDbehavior, the lack of differential improvement on most outcome measures, the absence of a clear effect of the adaptive training compared to the mock-training, and the high attrition rate suggest that the training in its present form is probably not suitable for children with ASD.

.....

J Clin Exp Neuropsychol. 2015 May;37:429-38.

COGNITION IN SCHOOL-AGED CHILDREN WITH "ACTIVE" EPILEPSY: A POPULATION-BASED STUDY. *Reilly C, Atkinson P, Das KB, et al.*

INTRODUCTION: There is a lack of population-based data on specific cognitive profiles in childhood epilepsy. This study sought to determine the frequency of impairments in global cognition and aspects of working memory and processing speed in a population-based sample of children with "active" epilepsy (on antiepileptic Drugs (AEDs), and/or had a seizure in the last year). Factors significantly associated with global and specific difficulties in cognition were also identified.

METHOD: A total of 85 (74% of eligible population) school-aged children (5-15 years) with "active" epilepsy underwent comprehensive psychological assessment including assessment of global cognition, working memory, and processing speed. Scores on cognitive subtests were compared via paired-samples t tests. The factors associated with cognitive difficulties were analyzed via linear regression.

RESULTS: A total of 24% of children were functioning below IQ 50, and 40% had IQ scores below 70. Scores on the Processing Speed Index were significantly lower than scores on the Verbal or Performance indexes on Wechsler instruments. The Coding subtest was a significant weakness compared with the other Wechsler subtests. A total of 58% of children displayed "memory underachievement" (memory score 1 SD below assessed IQ) on at least one of the four administered working memory subtests. Factors significantly associated with globally impaired cognition included being on polytherapy (beta = -13.0; 95% CI [-19.3, -6.6], p = .000) and having attention-deficit/hyperactivity disorder (ADHD; beta = -11.1, 95% CI [-3.0, -19.3], p = .008). Being on polytherapy was also associated with lower scores on the working memory and processing speed composite scores. Having developmental coordination disorder (DCD) was associated with a lower score on the processing speed composite.

CONCLUSIONS: There is a high rate of global and specific cognitive difficulties in childhood epilepsy. Difficulties are most pronounced in aspects of working memory and processing speed. Predictors of cognitive impairment in childhood epilepsy include epilepsy-related and behavioral factors, which may differ depending on the domain of cognition assessed.

.....

J Dev Behav Pediatr. 2015 May.

SOCIAL ADVERSITY AND REGIONAL DIFFERENCES IN PRESCRIBING OF ADHD MEDICATION FOR SCHOOL-AGE CHILDREN.

Wallach-Kildemoes H, Skovgaard AM, Thielen K, et al.

OBJECTIVES: To explore whether regional variations in the initiation of attention-deficit hyperactivity disorder (ADHD) medication among school-age children are explained by differences in sociodemographic composition and/or ADHD prescribing practice, especially in children who face social adversity (low parental education and single parenthood).

METHODS: A cohort of Danish school-age children (ages 5-17) without previous psychiatric conditions (N = 813,416) was followed during 2010-2011 for incident ADHD prescribing in the individual-level Danish registers. Register information was retrieved for both children and their parents. Regional differences were decomposed into contributions from differences in sociodemographic composition and in prescribing practices. Incidence rate ratios (IRR) with 95% confidence interval (CI) of ADHD prescribing were calculated using demographically standardized multivariable Poisson regression models.

RESULTS: Compared with the Capital, prescribing rates were significantly higher in regions North and Zealand (IRR, 1.19; 95% CI, 1.08-1.32 and 1.17; 1.08-1.28, respectively) and lower in South (IRR, 0.60; 95% CI, 0.54-0.66). After inclusion of the interaction term (region*social adversity), the multivariable analyses revealed a higher rate for the most disadvantaged children in North (IRR, 2.00; 95% CI, 1.51-2.66) and a lower rate in South (IRR, 0.47; 95% CI, 0.3-0.65). Prescribing rates were the highest for disadvantaged children in all regions, demonstrating the steepest social gradient in North and the smoothest in South. Demographic composition explained little of the variation: 3% for North and 13% for Zealand.

CONCLUSIONS: Differences in sociodemographic composition explain little of regional variation in incident ADHD prescribing for children. However, large regional differences prevail in prescribing practices for children facing social adversity, indicating that local cultures shape the interpretation and handling of children with ADHD-like behaviors

.....

J Pediatr. 2015 May;166:1297-302.

CLINICAL CORRELATES OF PARENTING STRESS IN CHILDREN WITH TOURETTE SYNDROME AND IN TYPICALLY DEVELOPING CHILDREN.

Stewart SB, Greene DJ, Lessov-Schlaggar CN, et al.

OBJECTIVE: To determine the impact of tic severity in children with Tourette syndrome on parenting stress and the impact of comorbid attention-deficit hyperactivity disorder (ADHD) and obsessive-compulsive disorder (OCD) symptomatology on parenting stress in both children with Tourette syndrome and typically developing children.

STUDY DESIGN: Children with diagnosed Tourette syndrome (n = 74) and tic-free typically developing control subjects (n = 48) were enrolled in a cross-sectional study.

RESULTS: Parenting stress was greater in the group with Tourette syndrome than the typically developing group. Increased levels of parenting stress were related to increased ADHD symptomatology in both children with Tourette syndrome and typically developing children. Symptomatology of OCD was correlated with parenting stress in Tourette syndrome. Parenting stress was independent of tic severity in patients with Tourette syndrome.

CONCLUSIONS: For parents of children with Tourette syndrome, parenting stress appears to be related to the child's ADHD and OCD comorbidity and not to the severity of the child's tic. Subthreshold ADHD symptomatology also appears to be related to parenting stress in parents of typically developing children. These findings demonstrate that ADHD symptomatology impacts parental stress both in children with and without a chronic tic disorder.

.....

J Pediatr. 2015 Jun;166:1423-30.

TREATMENT OF ATTENTION DEFICIT/HYPERACTIVITY DISORDER AMONG CHILDREN WITH SPECIAL HEALTH CARE NEEDS.

Visser SN, Bitsko RH, Danielson ML, et al.

OBJECTIVES: To describe the parent-reported prevalence of treatments for attention deficit/hyperactivity disorder (ADHD) among a national sample of children with special health care needs (CSHCN), and assess the alignment of ADHD treatment with current American Academy of Pediatrics guidelines.

STUDY DESIGN: Parent-reported data from the 2009-2010 National Survey of Children with Special Health Care Needs allowed for weighted national and state-based prevalence estimates of medication, behavioral therapy, and dietary supplement use for ADHD treatment among CSHCN aged 4-17 years with current ADHD. National estimates were compared across demographic groups, ADHD severity, and comorbidities. Medication treatment by drug class was described.

RESULTS: Of CSHCN with current ADHD, 74.0% had received medication treatment in the past week, 44.0% had received behavioral therapy in the past year, and 10.2% used dietary supplements for ADHD in the past year. Overall, 87.3% had received past week medication treatment or past year behavioral therapy
(both, 30.7%; neither, 12.7%). Among preschool-aged CSHCN with ADHD, 25.4% received medication treatment alone, 31.9% received behavioral therapy alone, 21.2% received both treatments, and 21.4% received neither treatment. Central nervous system stimulants were the most common medication class (84.8%) among CSHCN with ADHD, followed by the selective norepinephrine reuptake inhibitor atomoxetine (8.4%).

CONCLUSION: These estimates provide a benchmark of clinical practice for the period directly preceding issuance of the American Academy of Pediatrics' 2011 ADHD guidelines. Most children with ADHD received medication treatment or behavioral therapy; just under one-third received both. Multimodal treatment was most common for CSHCN with severe ADHD and those with comorbidities. Approximately one-half of preschoolers received behavioral therapy, the recommended first-line treatment for this age group.

.....

J Pediatr Psychol. 2015 May;40:455-63.

THE RELATIONSHIP BETWEEN WEIGHT STATUS AND EMOTIONAL AND BEHAVIORAL PROBLEMS IN SPANISH PRESCHOOL CHILDREN.

Perez-Bonaventura I, Granero R, Ezpeleta L.

OBJECTIVE: To examine cross-sectional and longitudinal associations between behavioral problems and weight status, considering body mass index (BMI) z-scores and overweight status, in a community sample of preschoolers.

METHODS: The Strengths and Difficulties Questionnaire and the Diagnostic Interview for Children and Adolescents were administered to 611 parents. Adjusted general linear models and binary logistic regressions were used.

RÉSULTS: Children who were overweight and had a higher BMI were at increased risk of peer problems and attention-deficit/hyperactivity disorder (ADHD) symptoms. Prospective analyses showed that a higher BMI at the age of 3 years was predictive of peer problems at ages 4 and 5 years and hyperactivity and ADHD symptoms at the age of 4 years.

CONCLUSION: This is the first study using a diagnostic-based instrument that shows a relationship between weight status and ADHD symptoms in preschoolers. Overweight children might benefit from screening for behavioral disorders and peer relationship problems.

.....

J Voice. 2015 May;29:287-91.

VOCAL FOLD NODULES IN SCHOOL AGE CHILDREN: ATTENTION DEFICIT HYPERACTIVITY DISORDER AS A POTENTIAL RISK FACTOR.

D'Alatri L, Petrelli L, Calo L, et al.

OBJECTIVE: To evaluate the presence of symptoms of inattention and hyperactivity/impulsivity in a population of school age children affected by vocal fold nodules.

METHODS: Parents and teachers of 18 children with vocal fold nodules (10 males, eight females; aged between 6 and 12 years) and 20 matched controls without dysphonia and/or vocal fold diseases (11 males, nine females; aged between 6 and 12 years) completed Attention-Deficit/Hyperactivity Disorder (ADHD) rating scale for parents (SDAG [Scala per i Disturbi di Attenzione/Iperattivita per Genitori]) and teachers (SDAI [Scala per i Disturbi di Attenzione/Iperattivita per Insegnanti) rating scales containing in two subscales items that specifically evaluate the symptoms of ADHD according to the DSM-IV. All children were subjected to videolaryngoscopy.

RESULTS: The group with vocal fold nodules scored significantly higher than the controls; the difference between the two groups was statistically significant for both the subscales of both questionnaires (SDAG and SDAI) (P < 0.05). Four children in the group with vocal fold nodules who scored higher than 14 in at least one subscale were referred for psychiatric evaluation. For two of the children, both male, a diagnosis of combined ADHD was formulated.

CONCLUSIONS: ADHD is a possible risk factor for the development of vocal fold nodules in childhood. SDAG and SDAI rating scales may supplement the diagnostic assessment of children with vocal fold nodules.

.....

JAMA Pediatr. 2015;169:391-95.

INJURY PREVENTION BY MEDICATION AMONG CHILDREN WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER A CASE-ONLY STUDY.

Mikolajczyk R, Horn J, Schmedt N, et al.

Importance: Children and adolescents with attention-deficit/hyperactivity disorder (ADHD) have an increased risk of injuries. Attention-deficit/hyperactivity disorder is often treated with medication, but the evidence regarding prevention of injuries is inconclusive.

Objective: To determine via a case-only design whether the use of methylphenidate hydrochloride or atomoxetine hydrochloride reduces the risk of injuries among children and adolescents with ADHD.

Design, Setting, And Participants: We used the German Pharmacoepidemiological Research Database, which includes records from about 17 million insurees (approximately 20% of the population) from 4 statutory health insurance providers in Germany to identify children aged 3 to 17 years with new diagnoses of ADHD in 2005 and 2006.We identified 37 650 children with ADHD based on inpatient and outpatient diagnostic codes (F90.0, F90.1, and F90.9) from the German modification of the International Statistical Classification of Diseases and Related Health Problems, 10th Revision. Among them, we identified those with an inpatient injury diagnosis during follow-up until 2009. A total of 2128 children with any injury diagnosis at hospitalization, 821 of whom had a brain injury diagnosis, were included in the analysis.We applied the self-controlled case series design to control for time-invariant characteristics of the patients and time trends in the exposure.

Exposures: Treatment with methylphenidate or atomoxetine based on prescription.

Main Outcomes And Measures: Hospitalization because of any injury or brain injury according to the injury mortality diagnosis matrix.

Results: Incidence rate ratios for the periods with medication compared with nonmedicated periods were 0.87 (95%Cl, 0.74-1.02) for hospitalization with any injuries and 0.66 (95%Cl, 0.48-0.91) for brain injuries only in the full sample. These estimates remained stable in sensitivity analyses restricting the sample to a narrower age range or to patients with a single hospitalization. There was no indication that medication prescriptions are increased after hospitalizations.

Conclusions and Relevance: No significant risk reduction for hospitalizations with injury diagnoses was observed during periods of ADHD medication, but there was a preventive effect on the risk of brain injuries (34%risk reduction). The effects were controlled for time-invariant characteristics of the patients by the study design.

.....

JAMA Psychiatry. 2015 May.

GENETIC AND ENVIRONMENTAL INFLUENCES ON THE DEVELOPMENTAL COURSE OF ATTENTION-DEFICIT/HYPERACTIVITY DISORDER SYMPTOMS FROM CHILDHOOD TO ADOLESCENCE.

Pingault JB, Viding E, Galera C, et al.

Importance: Attention-deficit/hyperactivity disorder (ADHD) is conceptualized as a neurodevelopmental disorder that is strongly heritable. However, to our knowledge, no study to date has examined the genetic and environmental influences explaining interindividual differences in the developmental course of ADHD symptoms from childhood to adolescence (ie, systematic decreases or increases with age). The reason ADHD symptoms persist in some children but decline in others is an important concern, with implications for prognosis and interventions.

Objective: To assess the proportional impact of genes and the environment on interindividual differences in the developmental course of ADHD symptom domains of hyperactivity/impulsivity and inattention between ages 8 and 16 years.

Design, Setting, and Participants: A prospective sample of 8395 twin pairs from the Twins Early Development Study, recruited from population records of births in England and Wales between January 1, 1994, and December 31, 1996. Data collection at age 8 years took place between November 2002 and November 2004; data collection at age 16 years took place between February 2011 and January 2013.

Main Outcomes and Measures: Both DSM-IV ADHD symptom subscales were rated 4 times by participants' mothers.

Results: Estimates from latent growth curve models indicated that the developmental course of hyperactivity/impulsivity symptoms followed a sharp linear decrease (mean score of 6.0 at age 8 years to 2.9 at age 16 years). Interindividual differences in the linear change in hyperactivity/impulsivity were under strong additive genetic influences (81%; 95% CI, 73%-88%). More than half of the genetic variation was specific to the developmental course and not shared with the baseline level of hyperactivity/impulsivity. The linear decrease in inattention symptoms was less pronounced (mean score of 5.8 at age 8 years to 4.9 at age 16 years). Nonadditive genetic influences accounted for a substantial amount of variation in the developmental course of inattention symptoms (54%; 95% CI, 8%-76%), with more than half being specific to the developmental course.

Conclusions and Relevance: The large genetic influences on the developmental course of ADHD symptoms are mostly specific and independent of those that account for variation in the baseline level of symptoms. Different sets of genes may be associated with the developmental course vs the baseline level of ADHD symptoms and explain why some children remit from ADHD, whereas others persist. Recent longitudinal imaging data indicate that the maintenance or increase in symptoms is underpinned by atypical trajectories of cortical development. This may reflect a specific genetic liability, distinct from that which contributes to baseline ADHD symptoms, and warrants closer follow-up.

.....

JBI Libr Syst Rev. 2014;12:41-53.

PARENTING EXPERIENCES OF LIVING WITH A CHILD WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER: A SYSTEMATIC REVIEW OF QUALITATIVE EVIDENCE PROTOCOL.

Laugesen B, Gronkjae M.

Review question/objective The objective of the systematic review is to identify and synthesize the best available evidence on how parents experience living with a child with attention deficit hyperactivity disorder including their experiences of attention deficit hyperactivity disorder health care services. The review questions are: How does living with a child with attention deficit hyperactivity disorder affect family life? What are the parental challenges of having a child with attention deficit hyperactivity disorder? How do parents experience collaboration with health care settings and professionals

Inclusion criteria Types of participants This review will consider studies that include parents living with a child with attention deficit hyperactivity disorder. For the purpose of the review, the definition of parents will be biological parents or persons with parental rights of the child. To investigate the phenomena of interest, the review will include studies examining the experiences of both mothers and fathers or single parents. Studies will be excluded if they examine other disorders or diseases than attention deficit hyperactivity disorder. In this review, a child is defined as a child or an adolescent living at home aged between five and 18 years. There will be no limits with regards to attention deficit hyperactivity disorder diagnostic criteria, as it is not the phenomena of interest in this study.

Phenomena of interest The phenomena of interest are parenting experiences of living with a child with attention deficit hyperactivity disorder to understand how the childnulls disorder affects family life. The phenomena of interest are also parenting experiences of attention deficit hyperactivity disorder health care services both in and outside of hospital settings and their experience of collaboration with professionals. Studies will be included if they entail parenting experiences of children already diagnosed with attention deficit hyperactivity disorder. Studies will be excluded if they investigate children who are not yet diagnosed with attention deficit hyperactivity disorder. Parenting attitudes to the attention deficit hyperactivity disorder diagnosis and parenting experiences with the time before their childnulls diagnosis will also be excluded.

The objective is not to investigate attention deficit hyperactivity disorder medication. Therefore, studies will be excluded if their focus is entirely on attitudes towards attention deficit hyperactivity disorder medication.

.....

J Bras Psiguiatr. 2015;64:90-91.

RELATIONSHIP BETWEEN THE PROFESSIONAL OF REFERENCE AND THE PERMANENCE OF **ADHD** PATIENTS IN A PSYCHOSOCIAL CARE CENTER FOR CHILDREN AND ADOLESCENTS IN MINAS GERAIS. *Guedes LA, Vital WC, Magalhaes CVA, et al.*

.....

J Abnorm Child Psychol. 2015 May;43:669-80.

NEUROPSYCHOLOGICAL HETEROGENEITY IN PRESCHOOL ADHD: INVESTIGATING THE INTERPLAY BETWEEN COGNITIVE, AFFECTIVE AND MOTIVATION-BASED FORMS OF REGULATION .

Sjöwall D, Backman A, Thorell LB.

There is a trend toward diagnosing ADHD prior to school entry. Despite this, there is a lack of studies investigating ADHD in the preschool years, at least studies including a large range of different neuropsychological functions. Our knowledge of the independent effects of different neuropsychological functions in relation to preschool ADHD is therefore limited. In order to address this issue, the present study investigated cognitive, affective, and motivation-based regulation in relation to ADHD symptoms in 104 preschool children (age M = 67.33 months, SD = 10.10; 65 % boys). Results showed that these regulatory processes were all significantly related to ADHD symptoms and that most of these relations remained after controlling for comorbid conduct problems. Most previous preschool studies have only included cognitive regulation, and to some extent motivation-based regulation. By also including affective regulation, we were able to explain a larger proportion of the variance in ADHD symptoms. However, it should be noted that the amount of variance explained was still small in comparison with what has been found in previous studies of school-aged children. This finding could be taken as an indication that further studies examining the nature of preschool ADHD are needed, and that it may be necessary to look beyond the neuropsychological factors that have been linked to the disorder in older children and adults.

.....

J Abnorm Child Psychol. 2015 May;43:681-91.

INSTRUMENTAL LEARNING IN ADHD IN A CONTEXT OF REWARD: INTACT LEARNING CURVES AND PERFORMANCE IMPROVEMENT WITH METHYLPHENIDATE.

Luman M, Goos V, Oosterlaan J.

We tested the hypothesis that instrumental learning is impaired in children with attention deficit/hyperactivity disorder (ADHD) and tested whether this deficiency can be ameliorated by the use of three different doses of methylphenidate (MPH): a low, a medium, and a high dose. Fifty children (23 with ADHD, 27 typically developing) performed an instrumental learning task in which they had to map four stimuli to two responses using feedback that differed in information value and that was coupled to monetary gain (O.2). Feedback was either contingent, thus fully informative on performance, or probabilistic, and informative in only 88 % of the trials. Dependent variables were response accuracy and latency. Contrary to predictions, children with ADHD and typically developing controls did not differ in their ability to acquire the stimulus–response mappings, in either condition. This indicates that with a simple instrumental learning task, children with ADHD are able to learn from rewarded feedback, as controls do, suggesting that children with ADHD are capable of learning both at home and in class when the environment is adequate. Possibly, learning problems are more evident in children with ADHD exhibited high levels of

parent-rated ODD symptoms. Medication analysis showed that children with ADHD completed the task more accurately and faster when taking MPH compared to placebo, particularly when the dose was high.

.....

J Adolesc. 2015;42:59-67.

ADOLESCENTS' BELIEFS ABOUT THE FAIRNESS OF EXCLUSION OF PEERS WITH MENTAL HEALTH PROBLEMS. O'Driscoll C, Heary C, Hennessy E, McKeague L.

Stigma research suggests that exclusion of peers with mental health problems is acceptable, however, no research has explored young people's beliefs about the fairness of exclusion. Group interviews with 148 adolescents explored judgements about the fairness of excluding peers with ADHD or depression from dyads and groups. Young people evaluated exclusion of peers with ADHD or depression from dyads and groups, with the exception of group exclusion of the peer with ADHD, as mostly unfair. Beliefs about the fairness of exclusion were influenced by the attributions that they applied to the target peer's behaviour, social obligations and loyalty within friendships and concerns about the adverse psychological effects of exclusion. Furthermore, their evaluations were influenced by personal beliefs about the social and personal costs of including the target peer. Evaluations of exclusion highlight novel avenues for to develop knowledge on the stigma of mental health problems.

.....

J Autism Dev Disord. 2015.

POVERTY AND THE GROWTH OF EMOTIONAL AND CONDUCT PROBLEMS IN CHILDREN WITH AUTISM WITH AND WITHOUT COMORBID ADHD.

Flouri E, Midouhas E, Charman T, et al.

We investigated the longitudinal relationship between socio-economic disadvantage (SED) and trajectories of emotional and conduct problems among children with autism spectrum disorder (ASD) who had comorbid attention deficit/hyperactivity disorder (ADHD; ASD + ADHD) or not (ASD null ADHD). The sample was 209 children with ASD who took part in the UKnulls Millennium Cohort Study. Trajectories of problems across ages 3, 5 and 7 years were analyzed using growth curve models. The ASD null ADHD group decreased in conduct problems over time but the ASD + ADHD group continued on a high trajectory. Although SED was not a risk factor for ASD + ADHD, it was associated with elevated emotional problems among children with ASD + ADHD. This effect of SED on emotional problems was not attenuated by parenting or peer problems.

.....

J Child Adolesc Psychopharmacol. 2015 Apr;25:269-71.

EFFICACY OF ATOMOXETINE FOR SYMPTOMS OF ATTENTION-DEFICIT/HYPERACTIVITY DISORDER IN CHILDREN WITH A HISTORY OF CHILD ABUSE.

Sugimoto A, Suzuki Y, Endo T, et al.

Objective: Recent studies suggest that the severity and drug response of depression and anxiety are correlated with childhood abuse. However, whether a history of child abuse can predict the severity and/or drug response of attention-deficit/ hyperactivity disorder (ADHD) is unclear. Therefore, we conducted a retrospective study to assess the efficacy of atomoxetine in children with a history of child abuse.

Methods: We reviewed 41 cases of children treated with atomoxetine. Specifically, we compared dissociation associating symptoms (DAS) and other symptoms (OS) measured via the ADHD Rating Scale (ADHD-RS) in abused and nonabused children at baseline and at 8 weeks after atomoxetine administration.

Results: At baseline, abused children had higher total scores $(38.7 \pm 9.3 \text{ vs. } 30.5 \pm 9.4, \text{ p} = 0.011)$, and greater levels of hyperactivity/impulsivity (17.3 ± 5.8 vs. 11.3 ± 6.0, p = 0.004) on the ADHD-RS than did nonabused children, whereas the inattention scores were similar between the two groups (21.4 ± 4.8 vs. 19.2 ± 4.6). Additionally, the total score and the two subscores decreased at week 8 for both groups. In the

nonabused group, DAS ($5.5 \pm 2.3 \text{ vs.} 3.9 \pm 1.7$, p < 0.001) and OS ($25.0 \pm 8.1 \text{ vs.} 17.4 \pm 6.7$, p < 0.001) significantly decreased after atomoxetine treatment. However, DAS in the abused group did not change after atomoxetine treatment ($5.9 \pm 2.3 \text{ vs.} 5.1 \pm 1.8$), whereas OS significantly decreased ($32.8 \pm 7.6 \text{ vs.} 25.7 \pm 7.2$, p = 0.002).

Conclusions: If DAS were caused by traumatic experiences in abused children, trauma treatment tools other than pharmacotherapy might be useful to treat DAS. These tools may include eye movement desensitization and reprocessing and traumafocused cognitive behavioral therapy.

.....

J Child Adolesc Psychopharmacol. 2015;25:246-53.

NEUROCOGNITIVE PERFORMANCE AND BEHAVIORAL SYMPTOMS IN PATIENTS WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER DURING TWENTY-FOUR MONTHS OF TREATMENT WITH METHYLPHENIDATE. Wang L-J, Chen C-K, Huang Y-S.

Objective: This study investigated the trends in neurocognitive function and behavioral symptoms among patients with attention-deficit/hyperactivity disorder (ADHD) during 24 months of treatment with methylphenidate in a clinical setting.

Methods: Study participants consisted of 181 ADHD patients with a mean age of 13.4(plus or minus)2.5 years (ages ranged from 8 to 18 years; 151 boys and 30 girls) who were prescribed oral short-acting methylphenidate two or three times daily, with each dose ranging between 0.3 and 1.0mg/kg. At baseline and 6, 12, 18, and 24 months from baseline, neurocognitive function was assessed using the Test of Variables of Attention (TOVA) on the day the patient was off medication, and behavioral symptoms were evaluated using the Swanson, Nolan, and Pelham Version IV Scale for ADHD (SNAP-IV) parent form, the SNAP-IV teacher form, and the ADHD-Rating Scale (completed by a child psychiatrist).

Results: Of the 181 ADHD patients at the initial visit, 103 (56.9%) completed the study. During the 24month methylphenidate treatment, only the commission errors in TOVA significantly improved; however, the omission errors, response time, response time variability, response sensitivity, and ADHD score did not. The behavioral symptoms of ADHD, observed by various informants, all declined substantially, and were significantly correlated with each other during the long-term follow-up. The severity of teacher ratings was lower than that of parent and psychiatrist ratings. However, the teacher-rated inattention symptoms showed the strongest correlations with TOVA performance.

Conclusions: Findings suggest that neurocognitive deficits in ADHD patients, except inhibition ability, might be long lasting in realistic settings. In addition, obtaining behavior profile assessments from multiple informants, especially from teachers, is vital for establishing a complete understanding of ADHD patients.

.....

J Child Adolesc Psychopharmacol. 2015;25:213-24.

COMORBID SYMPTOMATOLOGY MODERATES RESPONSE TO RISPERIDONE, STIMULANT, AND PARENT TRAINING IN CHILDREN WITH SEVERE AGGRESSION, DISRUPTIVE BEHAVIOR DISORDER, AND ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.

Farmer CA, Brown NV, Gadow KD, et al.

Objective: In this study, we evaluated parent and child characteristics as predictors and moderators of response in the four-site Treatment of Severe Childhood Aggression (TOSCA) study.

Methods: A total of 168 children with severe aggression, disruptive behavior disorder, and attentiondeficit/hyperactivity disorder (ADHD) were enrolled in a 9-week trial of basic treatment (n=84, stimulant + parent training + placebo) versus augmented treatment (n=84, stimulant + parent training + risperidone). In the initial report, augmented treatment surpassed basic treatment in reducing the primary outcome of disruptive behavior (D-Total) scores. In the current study, we evaluated parent (income, education, family functioning, employment) and child variables (intelligence quotient [IQ], aggression type, comorbid symptomatology) as predictors or moderators, using linear mixed models and the MacArthur guidelines.

Results: Higher scores on ADHD symptom severity and callous/unemotional traits predicted better outcome on D-Total regardless of treatment assignment. Two moderators of D-Total were found: Higher

anger/irritability symptoms and lower mania scores were associated with faster response, although not better overall effect at endpoint, in the augmented but not the basic group. Several variables moderated response on secondary outcomes (ADHD severity and prosocial behavior), and were characterized by faster response, although not better outcome, in the augmented but not in the basic group. Maternal education moderated outcome on the measure of positive social behavior; children of mothers with less education benefited more from augmented treatment relative to basic than those with more education. **Conclusion**: Although these findings require validation, they tentatively suggest that augmented treatment

works equally well across the entire sample. Nevertheless, certain child characteristics may be useful indicators for the speed of response to augmented treatment.

.....

J Child Adolesc Psychopharmacol. 2015;25:254-59.

TRENDS IN ATTENTION-DEFICIT/HYPERACTIVITY DISORDER DRUG CONSUMPTION IN CHILDREN AND ADOLESCENTS IN SLOVENIA FROM 2001 TO 2012: A DRUG USE STUDY FROM A NATIONAL PERSPECTIVE.

Stuhec M, Locatelli I, Svab V.

Objective: In most Eastern and Central European countries, except Germany, there is a lack of drug consumption studies for attention-deficit/hyperactivity disorder (ADHD). The main purpose of the present study was to present the pattern and the evolution of national ADHD drug consumption in Slovenia.

Methods: The national consumption data for the period 2001-2012 and medication costs were obtained from the database of the Health Insurance Institute of Slovenia. A defined daily dose (DDD) per 1000 inhabitants per day and the total medication cost in euro were extracted. Only immediate-release methylphenidate (IR-MPH), methylphenidate-osmotic release oral delivery system (OROS-MPH) and atomoxetine (ATX) have been approved for ADHD in Slovenia and are included in this study. Amphetamines have not been available in Slovenia.

Results: ADHD drug consumption increased in Slovenia from 0.0537 DDD/1000 inhabitants/day in 2001 to 0.0687 DDD/1000 inhabitants/day in 2006 and to 0.3076 DDD/1000 inhabitants/day in 2012. The rise was largely because of an increase in OROS-MPH consumption and increase in ATX consumption, whereas the consumption of IR-MPH decreased rapidly. During the study period, the total cost of the medicines increased 31-fold. From 2007 to 2010, the total cost of ADHD medicines increased 14-fold and from 2010 to 2012 the cost increased by 11.4% only.

Conclusions: When new drugs are licensed in a jurisdiction, their prescription rates increase rapidly. The changes in the pattern of prescribing medicines are evident in Slovenia, primarily in the increase of OROS-MPH and ATX prescriptions and in the rapid decrease of IR-MPH prescriptions. Results indicate a need for appropriate interventions in Slovenia.

.....

J Child Adolesc Psychopharmacol. 2015;25:203-12.

COMORBID ANXIETY AND SOCIAL AVOIDANCE IN TREATMENT OF SEVERE CHILDHOOD AGGRESSION: RESPONSE TO ADDING RISPERIDONE TO STIMULANT AND PARENT TRAINING; MEDIATION OF DISRUPTIVE SYMPTOM RESPONSE.

Arnold LE, Gadow KD, Farmer CA, et al.

Objective: In the four-site Treatment of Severe Childhood Aggression (TOSCA) study, addition of risperidone to stimulant and parent training moderately improved parent-rated disruptive behavior disorder (DBD) symptoms. This secondary study explores outcomes other than DBD and attention-deficit/hyperactivity disorder (ADHD) as measured by the Child and Adolescent Symptom Inventory-4R (CASI-4R).

Methods: A total of 168 children ages 6-12 with severe aggression (physical harm), DBD, and ADHD were randomized to parent training plus stimulant plus placebo (basic treatment) or parent training plus stimulant plus risperidone (augmented treatment) for 9 weeks. All received only parent training plus stimulant for the first 3 weeks, then those with room for improvement received a second drug (placebo or risperidone) for 6 weeks. CASI-4R category item means at baseline and week 9 were entered into linear mixed-effects

models for repeated measures to evaluate group differences in changes. Mediation of the primary DBD outcome was explored.

Results: Parent ratings were nonsignificant with small/negligible effects, but teacher ratings (n=46 with complete data) showed significant augmented treatment advantage for symptoms of anxiety (p=0.013, d=0.71), schizophrenia spectrum (p=0.017, d=0.45), and impairment in these domains (p=0.02, d=0.26), all remaining significant after false discovery rate correction for multiple tests. Improvement in teacher-rated anxiety significantly (p=0.001) mediated the effect of risperidone augmentation on the primary outcome, the Disruptive-total of the parent-rated Nisonger Child Behavior Rating Form.

Conclusions: Addition of risperidone to parent training plus stimulant improves not only parent-rated DBD as previously reported, but also teacher-rated anxiety-social avoidance. Improvement in anxiety mediates improvement in DBD, suggesting anxiety-driven fight-or-flight disruptive behavior with aggression, with implications for potential treatment strategies. Clinicians should attend to possible anxiety in children presenting with aggression and DBD.

Clinical Trial Registry: Treatment of Severe Childhood Aggression (The TOSCA Study). NCT00796302. clinicaltrials.gov

.....

J Child Adolesc Psychopharmacol. 2015;25:225-33.

PARTICIPANT SATISFACTION IN A STUDY OF STIMULANT, PARENT TRAINING, AND RISPERIDONE IN CHILDREN WITH SEVERE PHYSICAL AGGRESSION.

Rundberg-Rivera EV, Townsend LD, Schneider J, et al.

Objective: The purpose of this study was to examine the satisfaction of families who participated in the Treatment of Severe Childhood Aggression (TOSCA) study.

Methods: TOSCA was a randomized clinical trial of psychostimulant plus parent training plus placebo (basic treatment) versus psychostimulant plus parent training plus risperidone (augmented treatment) for children with severe physical aggression, disruptive behavior disorder, and attention-deficit/hyperactivity disorder. Parents completed a standardized Parent Satisfaction Questionnaire (PSQ).

Results: Of the 168 families randomized, 150 (89.3%) provided consumer satisfaction data. When they were asked if they would join the study again if they had the option to repeat, 136 (91%) said "yes," 11 (7%) said "maybe," and one (<1%) said "no." When asked if they would recommend the study to other parents with children having similar problems, 147 (98%) said "yes" and 3 (2%) said "maybe." Between 71% (rating one aspect of the Parent Training) and 96% (regarding the diagnostic interview) endorsed study procedures using the most positive response option. Asked if there were certain aspects of the study that they especially liked, 64 (43%) spontaneously reported parent training. Treatment assignment (basic vs. augmented) and responder status were not associated with reported satisfaction. However, responder status was strongly associated with parent confidence in managing present (p<0.001) and future (p<0.005) problem behaviors.

Conclusions: These findings indicate high levels of satisfaction with TOSCA study involvement and, taken together with previous pediatric psychopharmacology social validity studies, suggest high levels of support for the research experience. These findings may inform research bioethics and may have implications for deliberations of institutional review boards.

Trial Registry: Treatment of Severe Childhood Aggression (The TOSCA Study), NCT00796302, clinicaltrials.gov

.....

J Child Adolesc Psychopharmacol. 2015 Apr;25:272-75.

CALLOUS-UNEMOTIONAL TRAITS IN A CHILD WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER AND OPPOSITIONAL DEFIANT DISORDER: MANAGING MEDICATION AND EXPECTATIONS.

Shah LD, Coffey BJ.

Presents a case report of a 12 year old boy who carries a diagnosis of attention deficit/ hyperactivity disorder (ADHD), oppositional defiant disorder (ODD), and communication disorder referred by another

clinic for oppositional and destructive behaviors. This case represents a very commonly encountered challenge in child and adolescent psychiatry practice: how to manage conduct disordered behavior in the context of ADHD. A second issue is to identify any potential predictors of poor long-term outcome, such as substance abuse, legal problems, and/or antisocial personality disorder. Of particular concern in this case are S's callous unemotional traits. What evidence-based interventions are most likely to reduce bad outcomes, and in particular, what are the best psychopharmacological approaches?

.....

J Child Adolesc Psychopharmacol. 2015 Mar;25:188-90.

QUETIAPINE AND CLOZAPINE COMBINATION TREATMENT FOR TOURETTE'S SYNDROME IN AN ADOLESCENT BOY: POTENTIAL ROLE OF DOPAMINE SUPERSENSITIVITY IN LOSS OF TREATMENT RESPONSE. Lan CC, Liu CC, Chen YS.

Presents a case report of a 15-year-old boy who was diagnosed with Tourette's syndrome (TS) and attention-deficit/hyperactivity disorder (ADHD). His tic symptoms included motor tics of eye blinking, neck twitching, shoulder shrugging, blowing air, touching earlobe, hopping, and throat clearing. Initial treatment with clonidine 37.5 /mg/day and osmotic controlled release oral delivery system (OROS)-methylphenidate 36 mg/day were prescribed. The patient was sensitive to clonidine's side effect of drowsiness; therefore, it was difficult to increase the dosage further. An antipsychotic with risperidone 1.5mg/day was added 2 weeks later, and this regimen led to fair response in controlling both tics and ADHD symptoms. Unfortunately, at 12 years of age, his tics worsened significantly in both severity and frequency, and caused substantial distress in daily life. Risperidone was first increased to 4 mg/day with substantial improvement of tics observed the next month, but the patient's tics were once again exacerbated 3 months later. Olanzapine 10 mg/day then replaced risperidone, and a marked improvement of tics was noted within 1 month; however, the patient could not tolerate the daytime sedation effect and olanzapine was discontinued 3 months later. At age 14, the patient's motor tics became exacerbated yet again and vocal tics of coprolalia also developed. Haloperidol 3 mg/day was added while clozapine 100 mg/day was continued. Both the patient's motor and vocal tics markedly improved within 1 month but then gradually worsened in the following 3 months.

.....

Journal of Child Psychology and Psychiatry. 2015 May;56:521-29.

NEUROCOGNITIVE PREDICTORS OF SUBSTANCE USE DISORDERS AND NICOTINE DEPENDENCE IN ADHD PROBANDS, THEIR UNAFFECTED SIBLINGS, AND CONTROLS: A 4-YEAR PROSPECTIVE FOLLOW-UP.

Groenman AP, Oosterlaan J, Greven CU, et al.

Background: Attention-Deficit/Hyperactivity Disorder (ADHD) is a risk factor for substance use disorders (SUDs) and nicotine dependence (ND). Neurocognitive deficits may predict the increased risk of developing SUDs and nicotine dependence.

Methods: This study comprised three groups derived from the Dutch part of the International Multicenter ADHD Genetics (IMAGE) study: ADHD probands (n = 294), unaffected siblings (n = 161), and controls (n = 214). At baseline (age = 12.2), a range of neurocognitive functions was assessed including executive functions (inhibition, working memory, timing), measures of motor functioning (motor timing and tracking) and IQ. After a mean follow-up of 4.2 years, SUDs and ND were assessed.

Results: None of the neurocognitive functions predicted later SUDs or ND in ADHD probands, even after controlling for medication use and conduct disorder. Slower response inhibition predicted later nicotine dependence in unaffected siblings (OR = 2.06, 95% CI = 1.22-3.48), and lower IQ predicted increased risk for SUDs in controls (OR = 1.96, 95% CI = 1.12-3.44).

Conclusions: Cold executive functions, motor functioning, and IQ did not predict the elevated risk of SUDs and ND in ADHD. Future studies should target 'hot' executive functions such as reward processing as risk factors for SUDs or ND.

J Clin Psychiatry. 2015 Mar;76:e334-e341.

TIME TRENDS IN INCIDENCE RATES OF DIAGNOSED ATTENTION-DEFICIT/HYPERACTIVITY DISORDER ACROSS 16 YEARS IN A NATIONWIDE DANISH REGISTRY STUDY.

Jensen CM, Steinhausen HC.

Objective: To investigate time trends in incidence rates of first-time diagnosed attention-deficit/hyperactivity disorder (ADHD) in a nationwide sample aged 4-65 years across 16 years and identify potential contributing factors to these time trends.

Method: Incidence rates of first-time diagnosed ADHD based on ICD-10 criteria in Danish psychiatric hospitals per 100,000 person years (PY) were calculated for the total population, the 2 sexes, and 4 age groups using data from the Danish Psychiatric Central Research Registry and annual census data. Time trends and the role of contributing factors were analyzed and identified using joinpoint regression procedures by calculating annual percent changes for the time period 1995-2010.

Results: A total of 20,281 patients were diagnosed with ADHD and incidence rates increased from 7.3 to 91.2 per 100,000 PY during the study period. Joinpoint analysis suggested that incidence rates for diagnosed ADHD rapidly increased from 1998 to 2002, peaked from 2002 to 2008, and slowed down from 2008 to 2010. Contributing factors to the observed time trends were a general increase in patients seen in psychiatry for any mental disorder and an increased awareness and recognition of ADHD in females, adolescents, and adults.

Conclusions: These results provide empirical data needed in the public and professional debate often based on theoretical rather than empirical arguments. Results support the notion of increasing incidence rates of diagnosed ADHD and identify that contributing factors are a general increase in the number of patients assessed in psychiatry and an increased recognition of females, adolescents, and adults with ADHD.

.....

J Consult Clin Psychol. 2015 Apr;83:280-92.

EFFECTS OF BEHAVIORAL AND PHARMACOLOGICAL THERAPIES ON PEER REINFORCEMENT OF DEVIANCY IN CHILDREN WITH ADHD-ONLY, ADHD AND CONDUCT PROBLEMS, AND CONTROLS.

Helseth SA, Waschbusch DA, Gnagy EM, et al.

Objective: This study compared the unique and combined effects of evidence-based treatments for ADHD—stimulant medication and behavior modification—on children's rates of reinforcement for deviant peer behavior (RDPB).

Method: Using a within-subjects design, 222 elementary school-age children attending a summer treatment program, including 151 children with ADHD (127 male), with and without comorbid conduct problems, and 71 control children (57 male), received varying combinations of behavior modification (no, low-intensity, and high-intensity) and methylphenidate (placebo, 0.15 mg/kg, 0.30 mg/kg, and 0.60 mg/kg). RDPB was measured through direct observation and compared across all behavior modification and medication conditions.

Results: Children with ADHD reinforced the deviant behavior of their peers at a significantly higher rate than control children in the absence of either intervention. However, that difference largely disappeared in the presence of both behavior modification and medication. Both low and high-intensity behavior modification, as well as medium (0.30 mg/kg) and high (0.60 mg/kg) doses of methylphenidate, significantly reduced the rate of ADHD children's RDPB to levels similar to the control group.

Conclusions: Results indicate that although untreated children with ADHD do engage in RDPB at a greater rate than their non-ADHD peers, existing evidence-based interventions can substantially decrease the presence of RDPB, thereby limiting potential iatrogenic effects in group-based treatment settings.

J Consult Clin Psychol. 2015 Apr;83:293-303.

ELECTRODERMAL RESPONDING PREDICTS RESPONSES TO, AND MAY BE ALTERED BY, PRESCHOOL INTERVENTION FOR ADHD.

Beauchaine TP, Neuhaus E, Gatzke-Kopp LM, et al.

Objectives: To evaluate electrodermal activity (EDA) as a prospective biomarker of treatment response, to determine whether patterns of EDA are altered by treatment, and to assess oppositional defiant disorder (ODD) as a possible moderator of trajectories in EDA after an empirically supported behavioral intervention for attention-deficit hyperactivity disorder (ADHD) in preschool.

Method: Nonspecific fluctuations (NSFs) in skin conductance, which index sympathetic nervous system activity, were assessed among 4–6 year old children with ADHD (n = 99) before they participated with their parents in 1 of 2 versions of the Incredible Years intervention. All were reassessed at posttreatment, and a subgroup (n = 49) were assessed again at 1-year follow-up.

Results: No difference in pretreatment NSFs was observed between ADHD participants and a group of normal control children (n = 41). Nevertheless, among those with ADHD, fewer NSFs at pretest predicted poorer treatment response on 4 of 7 externalizing outcomes. Furthermore, treatment was associated with increasing NSFs across time, but not for those who scored high on ODD at pretest.

Conclusions: Low EDA appears to mark resistance to treatment among preschoolers with ADHD. Furthermore, although our study was not experimental, treatment was associated with longitudinal increases in EDA, which were not observed in a normal control group. This may suggest increased sensitivity to discipline, with positive implications for long term outcome. In contrast to treated participants as a whole, however, those who scored high on ODD at pretest exhibited reduced EDA over time.

.....

J Gen Intern Med. 2015;30:S319.

THE HEART OF ATTENTION DEFICIT.

Proctor PA, Montgomery T, Frank TA, et al.

LEARNING OBJECTIVE #1: Stimulant medications used in the treatment of ADHD can cause serious and potentially life-threatening side effects, including pulmonary hypertension.

LEARNING OBJECTIVE #2: Side effects of stimulant medications appear to be dose dependent, and care should be taken to use the lowest effective doses for treatment of ADHD.

CASE: A 19-year-old Caucasian man presented to the hospital after loss of consciousness and limb shaking lasting 1 min. Witnesses reported confusion after he regained consciousness. The event was preceded by sudden onset of dyspnea and inspiratory chest pain at rest. He endorsed 5 days of dry cough diagnosed as bronchitis and 2 years of exertional chest pain and dyspnea. Home medications were doxycycline, methylphenidate, and dexmethylphenidate. The patient's only medical history was attentiondeficit/hyperactivity disorder diagnosed in elementary school. He was adopted as an infant. His mother died due to complications of an unspecified cardiac condition after delivery. He denied alcohol, tobacco, or illicit drug use. On presentation, the patient was alert and well-appearing. His temperature was 98.9 (degrees)F. heart rate was 112, and blood pressure was 158/111. Examination revealed a split S2 with loud pulmonic component and a 1/6 systolic murmur over the left sternal border. Lungs were clear to auscultation. Blood counts and metabolic panel were unremarkable. A CT angiogram found no pulmonary embolus, but demonstrated perivascular ground-glass opacities and marked enlargement of the main pulmonary artery, right ventricle, right atrium, and inferior vena cava Symptoms resolved spontaneously 4 h after arrival. The patient was discharged with cardiology follow up, where echocardiography revealed a dilated, hypokinetic right ventricle with systolic pressure of 120 mmHg. Right heart catheterization confirmed severe pulmonary hypertension and cardiac index 1.76 L/min/m2. Methylphenidate and dexmethylphenidate were discontinued. Continuous treprostinil was started. He was hospitalized three more times in 5 months with similar symptoms. Repeat catheterization found no improvement of pulmonary vascular resistance. Six months ago treprostinil was increased to the maximum recommended dose. He has remained free of hospitalizations since then despite lifestylelimiting chest pain and dyspnea.

DISCUSSION: According to the CDC's 2011 National Survey of Children's Health, 11.0 % of US children between ages 4 and 17 years are diagnosed with Attention-Deficit/ Hyperactivity Disorder. Prevalence has increased from 7.8 % in 2003. More than 6 % are treated with stimulants. This patient was diagnosed with

attention-deficit/hyperactivity disorder in elementary school and had been on stimulant medications for eleven years. Prior clinic notes documented concern about high stimulant doses, although his regimen always fell within recommended dosing guidelines. One third of patients with idiopathic pulmonary hypertension report prior amphetamine or cocaine use. The odds ratio for prior stimulant use was 10.14 in patients with idiopathic disease compared to patients with known risk factors. A pathogenic mechanism linking stimulant use and pulmonary vascular disease has not been discovered. Proposed mechanisms include toxic endothelial injury, hypoxic insult, direct spasm, vasculitis, and dysregulation of vascular tone mediators. Amphetamines increase serum levels of serotonin, which is both a pulmonary vasoconstrictor and pulmonary artery smooth muscle mitogen. Stimulant medications carry a warning label recommending that anyone being considered for their use undergo screening for family history of sudden death or ventricular arrhythmia and physical examination to screen for cardiopulmonary abnormalities. Patients who develop exertional chest pain, syncope, or other symptoms suggestive of cardiac disease should undergo immediate cardiac evaluation.

.....

Journal of Latina/o Psychology. 2015 May;3:71-87. CULTURALLY ADAPTING PARENT TRAINING FOR LATINO YOUTH WITH ADHD: DEVELOPMENT AND PILOT.

Gerdes AC, Kapke TL, Lawton KE, et al.

Focus group data from Latino parents, research examining Latino cultural values, and recommendations from mental health providers working with Latino families were used to culturally adapt, an evidence-based parent training program for Latino youth with attention-deficit/hyperactivity disorder (ADHD). Session-specific, cultural adaptations were made to 5 sessions, and 2 sessions were completely replaced with newly developed, more culturally congruent sessions. The adapted treatment also resulted in global adaptations to all treatment sessions, cultural adaptations to the assessment and feedback phase, as well as adaptations targeting practical barriers to treatment. Initial treatment outcomes from a small pilot demonstrated that 100% of families successfully completed the culturally adapted parent training program and reported being very satisfied with treatment. Eighty percent of children demonstrated reliable improvement in parent-reported ADHD symptomatology, and 40% of parents reported reliable improvement in both parental and family functioning.

.....

J Psychiatr Res. 2015;64:59-66.

MOTOR VEHICLE DRIVING IN HIGH INCIDENCE PSYCHIATRIC DISABILITY: COMPARISON OF DRIVERS WITH ADHD, DEPRESSION, AND NO KNOWN PSYCHOPATHOLOGY.

Aduen PA, Kofler MJ, Cox DJ, et al.

Although not often discussed in clinical settings, motor vehicle driving is a complex multitasking endeavor during which a momentary attention lapse can have devastating consequences. Previous research suggests that drivers with high incidence psychiatric disabilities such as ADHD contribute disproportionately to collision rates, which in turn portend myriad adverse social, financial, health, mortality, and legal outcomes. However, self-referral bias and the lack of psychiatric comparison groups constrain the generalizability of these findings. The current study addressed these limitations and examined the unique associations among ADHD, Depression, and adverse driving outcomes, independent of self-selection, driving exposure, and referral bias. The Strategic Highway Research Program (SHRP-2) Naturalistic Driving Study comprises U.S. drivers from six sites selected via probability-based sampling. Groups were defined by Barkley ADHD and psychiatric diagnosis questionnaires, and included ADHD (. n=275), Depression (. n=251), and Healthy Control (. n=1828). Primary outcomes included self-reported traffic collisions, moving violations, collision-related injuries, and collision fault (last 3 years). Accounting for demographic differences. ADHD but not Depression portended increased risk for multiple violations (OR=2.3) and multiple collisions (OR=2.2). ADHD but not Depression portended increased risk for collision fault (OR=2.1). Depression but not ADHD predicted increased risk for self-reported injury following collisions (OR=2.4). ADHD appears uniquely associated with multiple collisions, multiple violations, and collision fault, whereas Depression is uniquely associated with self-reported injury following a collision. Identification of the specific mechanisms underlying this risk will be critical to designing effective interventions to improve long-term functioning for drivers with high incidence psychiatric disability.

.....

J Psychiatr Res. 2015 May;64:40-50.

MULTIPLE EPIGENETIC FACTORS PREDICT THE ATTENTION DEFICIT/HYPERACTIVITY DISORDER AMONG THE CHINESE HAN CHILDREN.

Xu Y, Chen XT, Luo M, et al.

Attention deficit/hyperactivity disorder (ADHD) is one of the most common psychiatric disorders of childhood. Despite its prevalence, the critical factors involved in its development remain to be identified. It was recently suggested that epigenetic mechanisms probably contribute to the etiology of ADHD. The present study was designed to examine the associations of epigenetic markers with ADHD among Chinese Han children, aiming to establish the prediction model for this syndrome from the epigenetic perspective. We conducted a pair-matching case-control study, and the ADHD children were systematically evaluated via structured diagnostic interviews, including caregiver interviews, based on the Diagnostic and Statistical Manual of Mental Disorders, 4th edition, revised criteria (DSM-IV-R). The expression levels of risk genes DAT1, DRD4, DRD5, as well as their promoter methylation, were determined respectively, followed by the expression profiles of histone-modifying genes p300, MYST4, HDAC1, MeCP2. The multivariate logistic regressions were performed to establish ADHD prediction models. All of the seven genes tested were identified as risk factors for ADHD. The methylation of one critical CpG site located upstream of DRD4 was shown to affect its transcription, suggesting a role in ADHD's development. Aberrant DNA methylation and histone acetylation were indicated in ADHD patients. In addition, a prediction model was established using the combination of p300, MYST4 and HDAC1, with the accuracy of 0.9338. This is, to our knowledge, the first study to clearly demonstrate the associations between epigenetic markers and ADHD, shedding light on the preliminary diagnosis and etiological studies of this widespread disorder.

.....

J Am Acad Child Adolesc Psychiatry. 2015;54:394-402.

INCREASED NEURAL RESPONSES TO REWARD IN ADOLESCENTS AND YOUNG ADULTS WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER AND THEIR UNAFFECTED SIBLINGS.

von RD, Cools R, Zwiers MP, et al.

Objective Attention-deficit/hyperactivity disorder (ADHD) is a heritable neuropsychiatric disorder associated with abnormal reward processing. Limited and inconsistent data exist about the neural mechanisms underlying this abnormality. Furthermore, it is not known whether reward processing is abnormal in unaffected siblings of participants with ADHD.

Method We used event-related functional magnetic resonance imaging (fMRI) to investigate brain responses during reward anticipation and receipt with an adapted monetary incentive delay task in a large sample of adolescents and young adults with ADHD (n = 150), their unaffected siblings (n = 92), and control participants (n = 108), all of the same age.

Results Participants with ADHD showed, relative to control participants, increased responses in the anterior cingulate, anterior frontal cortex, and cerebellum during reward anticipation, and in the orbitofrontal, occipital cortex and ventral striatum. Responses of unaffected siblings were increased in these regions as well, except for the cerebellum during anticipation and ventral striatum during receipt.

Conclusion ADHD in adolescents and young adults is associated with enhanced neural responses in frontostriatal circuitry to anticipation and receipt of reward. The findings support models emphasizing aberrant reward processing in ADHD, and suggest that processing of reward is subject to familial influences. Future studies using standard monetary incentive delay task parameters are needed to replicate our findings.

J Am Acad Child Adolesc Psychiatry. 2015;54:360-68.

CHILDHOOD BEHAVIOR PROBLEMS AND ACADEMIC OUTCOMES IN ADOLESCENCE: LONGITUDINAL POPULATION-BASED STUDY.

Sayal K, Washbrook E, Propper C.

Objective To investigate the impact of increasing levels of inattention, hyperactivity/impulsivity, and oppositional/defiant behaviors at age 7 years on academic achievement at age 16 years.

Method In a population-based sample of 7-year-old children in England, information was obtained about inattention, hyperactivity/impulsivity, and oppositional/defiant behaviors (using parent and teacher ratings) and the presence of attention-deficit/hyperactivity disorder (ADHD) and disruptive behavior disorders (DBDs). After adjusting for confounder variables, their associations with academic achievement in national General Certificate of Secondary Education (GCSE) examinations (using scores and minimum expected school-leaving qualification level [5 "good" GCSEs]) at age 16 years were investigated (N = 11,640).

Results In adjusted analyses, there was a linear association between each 1-point increase in inattention symptoms and worse outcomes (2- to 3-point reduction in GCSE scores and 6% to 7% (10%-12% with teacher ratings) increased likelihood of not achieving 5 good GCSEs). ADHD was associated with a 27- to 32-point reduction in GCSE scores and, in boys, a more than 2-fold increased likelihood of not achieving 5 good GCSEs. In boys, oppositional/defiant behaviors were also independently associated with worse outcomes, and DBDs were associated with a 19-point reduction in GCSE scores and a 1.83-increased likelihood of not achieving 5 good GCSEs.

Conclusion Across the full range of scores at a population level, each 1-point increase in inattention at age 7 years is associated with worse academic outcomes at age 16. The findings highlight long-term academic risk associated with ADHD, particularly inattentive symptoms. After adjusting for inattention and ADHD respectively, oppositional/defiant behaviors and DBDs are also independently associated with worse academic outcomes.

.....

J Voice. 2015.

VOCAL HYPERFUNCTION IN PARENTS OF CHILDREN WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER. *Teresa G-R, Diaz-Roman TM.*

Objective: The objective of this study was to evaluate the presence of habits and symptoms of vocal hyperfunction in the parents of children with attention deficit hyperactivity disorder (ADHD).

Methods: Parents of 24 children with ADHD and 30 children of a control group completed a specific questionnaire to detect the hyperfunctional use of the voice (excessive talking, excessive loudness, talking too fast, and shouting), hoarseness, vocal fatigue, mental and physical fatigue, and the degree of parental concern for the vocal health of their child.

Results: Parents of children with ADHD spoke more often, faster, and stronger than the parents of the control group; in addition, they also used a louder volume than they usually used when they spoke to their children. The parents manifested more vocal, mental, and physical fatigue than the parents of the control group. There was a significant correlation between the "concern" for the vocal health of their children with respect to vocal symptoms of the children, the habits of vocal hyperfunctioning, and the symptoms suffered by the parents.

Conclusions: These results suggest that the parents of children with ADHD change their vocal attitude when communicating with their children. Most likely, the increased concern of parents with ADHD children and their respective level of stress lead to hyperfunctional vocal usage. This subsequently leads to symptoms of vocal, physical, and mental fatigue at the end of the day.

Medicine. 2015;94.

ENTEROVIRUS ENCEPHALITIS INCREASES THE RISK OF ATTENTION DEFICIT HYPERACTIVITY DISORDER: A TAIWANESE POPULATION-BASED CASE-CONTROL STUDY.

Chou I-C, Lin C-C, Kao C-H.

Enterovirus (EV) infection is a major public health issue throughout the world with potential neurological complications. This study evaluated the relationship between attention deficit hyperactivity disorder (ADHD) and EV encephalitis in children. Data of reimbursement claims from the National Health Insurance Research Database of Taiwan were used in a population-based case-control design. The study comprised 2646 children with ADHD who were matched according to sex, age, urbanization level of residence, parental occupation, and baseline year, to people without ADHD at a ratio of 1:10. The index date of the ADHD group was the ADHD date of diagnosis. Histories of EV infections before the index dates were collected and recategorized according to the severity of infection. Compared with children without EV infection, the children with mild EV infection had a 1.16-fold increased risk of ADHD (odds ratio [OR]=1.16, 95% confidence interval [CI]=1.07-1.26), and the children with severe EV infection had a greater risk of ADHD (OR=2.82, 95% CI=1.05-7.57). The results also revealed a significant correlation between ADHD and the severity of EV infection (P for trend=0.0001). Patients with EV encephalitis have an increased risk of developing ADHD. Although most EV encephalitis in children has a favorable prognosis, it may be associated with significant long-term neurological sequelae, even in children considered fully recovered at discharge. Neuropsychological testing should be recommended for survivors of childhood EV encephalitis. The causative factors between EV encephalitis and the increased risk of ADHD require further investigation.

Minerva Pediatr. 2015 May.

STRESS LEVELS IN PARENTS OF CHILDREN WITH AND WITHOUT ATTENTION-DEFICIT/HYPERACTIVITY DISORDER DURING THE BACK-TO-SCHOOL PERIOD: RESULTS OF AN INTERNATIONAL SURVEY IN ITALY.

.....

Loprieno U, Gagliano A.

AIM: The back-to-school stress survey was an international, non-clinical opinion survey, which aimed to compare stress levels in parents of children with/without attention- deficit/hyperactivity disorder (ADHD) during the back-to-school period. Here, we present results relating to the Italian sample, comparing them with European data.

METHODS: The questionnaire was built using a modified Holmes and Rahe stress scale. Parents of children with/without ADHD evaluated potentially stress-causing situations on a scale from 1 (low stress) to 10 (high stress).

RESULTS: In Italy, 107 parents of children with ADHD (mean age [SD]: 40.3 [7.3] years) and 105 parents of children without ADHD (mean age [SD]: 42.2 [6.6] years) participated in the survey. The mean age (SD) of children with ADHD was 10.3 (3.1) years; 77.6% were male, 72.9% had been diagnosed with at least one comorbid condition - in particular conduct disorder (24.3%), learning disorders/dyslexia (23.4%) and language/communication disorder (19.6%) - and 32.7% were receiving ADHD medication. Parents of children with ADHD showed significantly higher stress levels (p

CONCLUSIONS: Parents of children with ADHD suffer significantly higher stress levels compared with parents of children without ADHD. Considering parental stress is important for the management of children with ADHD, as stress can affect the control of behavioural symptoms of children.

NCHS Data Brief. 2015 May;1-8.

Association between diagnosed ADHD and selected characteristics among children aged 4-17 years: United States, 2011-2013.

Pastor P, Reuben C, Duran C, et al.

KEY FINDINGS: In 2011-2013, 9.5% of children aged 4-17 years were ever diagnosed with attention deficit hyperactivity disorder (ADHD). For those aged 4-5, prevalence was 2.7%, 9.5% for those aged 6-11, and 11.8% for those aged 12-17. Among all age groups, prevalence of ever diagnosed ADHD was more than twice as high in boys as girls. Among those aged 6-17, prevalence was highest among non-Hispanic white children and lowest among Hispanic children. Among all age groups, prevalence was higher among children aged 4-11, prevalence was higher for children with family income less than 200% of the federal poverty threshold than for children with family income at 200% or more of the poverty threshold.

.....

Neuropsychiatr Dis Treat. 2015;11:1169-74.

EVALUATION OF ACUTE CARDIOVASCULAR EFFECTS OF IMMEDIATE-RELEASE METHYLPHENIDATE IN CHILDREN AND ADOLESCENTS WITH ATTENTION-DEFICIT HYPERACTIVITY DISORDER.

Lamberti M, Italiano D, Guerriero L, et al .

Attention-deficit hyperactivity disorder is a frequent condition in children and often extends into adulthood. Use of immediate-release methylphenidate (MPH) has raised concerns about potential cardiovascular adverse effects within a few hours after administration. This study was carried out to investigate acute effects of MPH on electrocardiogram (ECG) in a pediatric population. A total of 54 consecutive patients with attention-deficit hyperactivity disorder (51 males and 3 females; mean age =12.14(plus or minus)2.6 years, range 6null19 years), receiving a new prescription of MPH, underwent a standard ECG 2 hours before and after the administration of MPH 10 mg per os. Basal and posttreatment ECG parameters, including mean QT (QT interval when corrected for heart rate [QTc]), QTc dispersion (QTd) interval duration, T-peak to Tend (TpTe) intervals, and TpTe/QT ratio were compared. Significant modifications of both QTc and QTd values were not found after drug administration. QTd fluctuated slightly from 25.7(plus or minus)9.3 milliseconds to 25.1(plus or minus)8.4 milliseconds; QTc varied from 407.6(plus or minus)12.4 milliseconds to 409.8(plus or minus)12.7 milliseconds. A significant variation in blood pressure (systolic blood pressure 105.4(plus or minus)10.3 vs 109.6(plus or minus)11.5; P<0.05; diastolic blood pressure 59.2(plus or minus)7.1 vs 63.1(plus or minus)7.9; P<0.05) was observed, but all the data were within normal range. Heart rate moved from 80.5(plus or minus)15.5 bpm to 87.7(plus or minus)18.8 bpm. No change in TpTe values was found, but a statistically significant increase in TpTe/QTc intervals was found with respect to basal values (0.207(plus or minus)0.02 milliseconds vs 0.214(plus or minus)0.02 milliseconds; P<0.01). The findings of this study show no significant changes in ECG parameters. TpTe values can be an additional parameter to evaluate borderline cases.

.....

Neuropsychology. 2015.

FUNCTIONAL MRI REVEALS DIFFERENT RESPONSE INHIBITION BETWEEN ADULTS AND CHILDREN WITH ADHD. Lei D, Du M, Wu M, et al.

Objective: Attention-deficit hyperactivity disorder (ADHD) has been recognized as a disorder of executive function, and a number of functional MRI (fMRI) studies have been conducted to investigate the altered brain activation patterns between ADHD patients and healthy controls. However, the findings across different studies have been inconsistent, and the different neural mechanisms between adults and children with ADHD remain unclear. The aim of this study was to perform a meta-analysis of fMRI studies to further investigate and compare the abnormalities in adults and children with ADHD during motor response inhibition.

Method: Activation likelihood estimation (ALE) was used to investigate brain activation differences between ADHD patients and controls, and a subtraction meta-analysis was performed to compare adult and child patients.

Results: Twenty-three studies met the inclusion criteria. Meta-analysis using ALE detected significantly decreased activation during response inhibition in ADHD in the supplementary motor area, insula, caudate, and precentral gyrus, as well as increased activation in the postcentral gyrus, inferior frontal gyrus, and precuneus. The activation decreases in the right caudate were greater in child ADHD patients than adult ADHD patients.

Conclusions: This meta-analysis identified dysfunction in several areas of the motor inhibition network that may play a role in the abnormal neural mechanisms of response inhibition in ADHD. The comparison of child and adult subgroups raises the possibility that the persistence of functional abnormalities of the caudate may be an important factor in whether ADHD persists.

.....

Neuropsychology. 2015;29:445-53.

EVERYDAY EXECUTIVE FUNCTION IMPAIRMENTS PREDICT COMORBID PSYCHOPATHOLOGY IN AUTISM SPECTRUM AND ATTENTION DEFICIT HYPERACTIVITY DISORDERS.

Lawson RA, Papadakis AA, Higginson CI, et al.

Objective: Autism spectrum disorder (ASD) and attention deficit hyperactivity disorder (ADHD) both have psychiatric comorbidities and distinctive profiles of executive dysfunction. Although there is evidence that executive function (EF) plays a role in the expression of specific behaviors and psychiatric symptoms, it is not known whether specific EF deficits in ASD and ADHD may be pathways to comorbidities in the disorders. This study examines whether parent reported problems with flexibility in ASD and inhibition in ADHD mediate the disorders' associations with anxiety/depression and oppositional/ aggressive behavior, respectively.

Method: Parent report data from the Behavior Rating Inventory of Executive Function (BRIEF) and the Child Behavior Checklist (CBCL) were obtained for 125 children (70 ASD, 55 ADHD Hyperactive/Impulsive or Combined type) as part of a neuropsychological assessment. Diagnostic status, BRIEF Shift (shifting/flexibility) and Inhibit (behavioral inhibition) scale scores, and CBCL Anxious/Depressed (anxiety/depression) and Aggressive Behavior (oppositionality/ aggression) scale scores were analyzed with a path analysis to investigate the relation of flexibility and inhibition to comorbid symptoms in children with ASD and ADHD.

Results: In a path model with good fit ASD predicted greater inflexibility which predicted greater anxiety/depression, while ADHD predicted greater disinhibition that predicted greater aggression, consistent with our mediational hypotheses. Unexpectedly, the greater inflexibility associated with ASD also predicted greater aggression.

Conclusions: Findings support the importance of everyday EF problems in ASD and ADHD as predictors of comorbid psychopathology and as crucial intervention targets for potential prevention and mitigation of comorbid symptoms.

.....

Neuropsychopharmacology. 2015 Jun;40:1717-25.

NEURAL CORRELATES OF AGGRESSION IN MEDICATION-NAIVE CHILDREN WITH ADHD: MULTIVARIATE ANALYSIS OF MORPHOMETRY AND TRACTOGRAPHY.

Cha J, Fekete T, Siciliano F, et al.

Aggression is widely observed in children with attention deficit/hyperactivity disorder (ADHD) and has been frequently linked to frustration or the unsatisfied anticipation of reward. Although animal studies and human functional neuroimaging implicate altered reward processing in aggressive behaviors, no previous studies have documented the relationship between fronto-accumbal circuitry-a critical cortical pathway to subcortical limbic regions-and aggression in medication-naive children with ADHD. To address this, we collected behavioral measures and parental reports of aggression and impulsivity, as well as structural and

diffusion MRI, from 30 children with ADHD and 31 healthy controls (HC) (mean age, 10+/-2.1 SD). Using grey matter morphometry and probabilistic tractography combined with multivariate statistical modeling (partial least squares regression and support vector regression), we identified anomalies within the frontoaccumbal circuit in childhood ADHD, which were associated with increased aggression. More specifically, children with ADHD showed reduced right accumbal volumes and frontal-accumbal white matter connectivity compared with HC. The magnitude of the accumbal volume reductions within the ADHD group was significantly correlated with increased aggression, an effect mediated by the relationship between the accumbal volume and impulsivity. Furthermore, aggression, but not impulsivity, was significantly explained by multivariate measures of fronto-accumbal white matter connectivity and cortical thickness within the orbitofrontal cortex. Our multi-modal imaging, combined with multivariate statistical modeling, indicates that the fronto-accumbal circuit is an important substrate of aggression in children with ADHD. These findings suggest that strategies aimed at probing the fronto-accumbal circuit may be beneficial for the treatment of aggressive behaviors in childhood ADHD.

Neuropsychopharmacology. 2015 May.

NEUROIMAGING-AIDED PREDICTION OF THE EFFECT OF METHYLPHENIDATE IN CHILDREN WITH ATTENTION-DEFICIT HYPERACTIVITY DISORDER: A RANDOMIZED CONTROLLED TRIAL.

.....

Ishii-Takahashi A, Takizawa R, Nishimura Y, et al .

Although methylphenidate hydrochloride (MPH) is a first-line treatment for children with attention-deficit hyperactivity disorder (ADHD), the non-response rate is 30%. Our aim was to develop a supplementary neuroimaging biomarker for predicting the clinical effect of continuous MPH administration by using nearinfrared spectroscopy (NIRS). After baseline assessment, we performed a double-blind, placebo-controlled, crossover trial with a single dose of MPH, followed by a prospective 4-to-8-week open trial with continuous MPH administration, and an ancillary 1-year follow-up. Twenty-two drug-naive and eight previously treated children with ADHD (NAIVE and NON-NAIVE) were compared with 20 healthy controls (HCs) who underwent multiple NIRS measurements without intervention. We tested whether NIRS signals at the baseline assessment or DeltaNIRS (single dose of MPH minus baseline assessment) predict the Clinical Global Impressions-Severity (CGI-S) score after 4-to-8-week or 1-year MPH administration. The secondary outcomes were the effect of MPH on NIRS signals after single-dose, 4-to-8-week, and 1-year administration. DeltaNIRS significantly predicted CGI-S after 4-to-8-week MPH administration. The leaveone-out classification algorithm had 81% accuracy using the NIRS signal. DeltaNIRS also significantly predicted CGI-S scores after 1 year of MPH administration. For secondary analyses, NAIVE exhibited significantly lower prefrontal activation than HCs at the baseline assessment, whereas NON-NAIVE and HCs showed similar activation. A single dose of MPH significantly increased activation compared with the placebo in NAIVE. After 4-to-8-week administration, and even after MPH washout following 1-year administration, NAIVE demonstrated normalized prefrontal activation. Supplementary NIRS measurements may serve as an objective biomarker for clinical decisions and monitoring concerning continuous MPH treatment in children with ADHD.Neuropsychopharmacology advance online publication, 27 May 2015; doi:10.1038/npp.2015.128

.....

Nutrition. 2015.

PROTECTIVE EFFECTS OF DIETARY SUPPLEMENTATION WITH NATURAL (OMEGA)-3 POLYUNSATURATED FATTY ACIDS ON THE VISUAL ACUITY OF SCHOOL-AGE CHILDREN WITH LOWER IQ OR ATTENTION-DEFICIT HYPERACTIVITY DISORDER.

Wu Q, Zhou T, Ma L, et al .

Objective: Little attention has been paid to the possible protective role of (omega)-3 polyunsaturated fatty acids (PUFAs) on the visual acuity of school-age children with lower IQs or attention-deficit hyperactivity disorder (ADHD). The aim of this study was to evaluate the effect of dietary (omega)-3 PUFAs on the visual acuity and red blood cell (RBC) fatty acid compositions of these children.

Methods: We randomly assigned 179 children with lower IQs or ADHD to receive ordinary eggs (control group, n=90) or eggs rich in C18:3 (omega)-3, eicosapentaenoic acid (EPA, 20:5 (omega)-3) and docosahexaenoic acid (DHA, 22:6 (omega)-3) for 3mo (study group, n=89). Before and after the intervention, distance visual acuity was tested using an E chart and the RBC fatty acid composition was determined using capillary gas chromatography.

Results: Three months later, 171 children completed the follow-up with the exception of 8 children who were unavailable during follow-up. Both groups of children showed a significant improvement in visual acuity (P<0.05), however, visual acuity in the study group was significantly better than that of the control group (P=0.013). The C18:3 (omega)-3 (P=0.009), DHA (P=0.009) and (summation sign)(omega)-3 (P=0.022) levels of the intervention group were significantly higher than those of the control group, while the C20:4 (omega)-6 (P=0.003), C22:4 (omega)-6 (P=0.000), (summation sign)(omega)-6 (P=0.001), (summation sign)(omega)-6/(summation sign)(omega)-3 (P=0.000) and arachidonic acid/DHA (P=0.000) of the study group were significantly lower than those of the control group. No significant differences in the levels of C18:2 (omega)-6 (P=0.220), C20:2 (omega)-6 (P=0.249), C20:3 (omega)-6 (P=0.258), C20:5 (omega)-3 (P=0.051), or C22:5 (P=0.200) were found between the two groups.

Conclusions: Dietary supplementation with (omega)-3 PUFAs improves both visual acuity and the RBC fatty acid profile in school-age children with lower IQs or ADHD.

.....

Pediatr Res. 2015 Jun;77:823-28.

A POSSIBLE LINK BETWEEN EARLY PROBIOTIC INTERVENTION AND THE RISK OF NEUROPSYCHIATRIC DISORDERS LATER IN CHILDHOOD: A RANDOMIZED TRIAL.

Partty A, Kalliomaki M, Wacklin P, et al.

BACKGROUND: Recent experimental evidence suggests that gut microbiota may alter function within the nervous system providing new insight on the mechanism of neuropsychiatric disorders.

METHODS: Seventy-five infants who were randomized to receive Lactobacillus rhamnosus GG (ATCC 53103) or placebo during the first 6 mo of life were followed-up for 13 y. Gut microbiota was assessed at the age of 3 wk, 3, 6, 12, 18, 24 mo, and 13 y using fluorescein in situ hybridization (FISH) and qPCR, and indirectly by determining the blood group secretor type at the age of 13 y. The diagnoses of attention deficit hyperactivity disorder (ADHD) and Asperger syndrome (AS) by a child neurologist or psychiatrist were based on ICD-10 diagnostic criteria.

RESULTS: At the age of 13 y, ADHD or AS was diagnosed in 6/35 (17.1%) children in the placebo and none in the probiotic group (P = 0.008). The mean (SD) numbers of Bifidobacterium species bacteria in feces during the first 6 mo of life was lower in affected children 8.26 (1.24) log cells/g than in healthy children 9.12 (0.64) log cells/g; P = 0.03.

CONCLUSION: Probiotic supplementation early in life may reduce the risk of neuropsychiatric disorder development later in childhood possible by mechanisms not limited to gut microbiota composition.

.....

Pediatr Res. 2015 May.

EFFICACY AND SAFETY OF ACUPUNCTURE IN CHILDREN: AN OVERVIEW OF SYSTEMATIC REVIEWS. Yang C, Hao Z, Zhang L, et al.

BACKGROUND: In recent years, acupuncture has increasingly being integrated into pediatric health care. It was used on approximately 150,000 children (0.2%).

METHODS: We aim to update the evidence for the efficacy and safety of acupuncture for children and evaluate the methodological qualities of these studies to improve future research in this area.

RESULTS: We included 24 systematic reviews, comprising 142 RCTs with 12787 participants. Only 25% (6/24) reviews were considered to be high quality (10.00 +/- 0.63). High-quality systematic reviews and Cochrane systematic reviews tends to yield neutral or negative results (P=0.052, 0.009 respectively). The efficacy of acupuncture for five diseases (Cerebral Palsy (CP), nocturnal enuresis, tic disorders, amblyopia and pain reduction) is promising. It was unclear for Hypoxic Ischemic Encephalopathy (HIE), Attention

Deficit Hyperactivity Disorder (ADHD), mumps, Autism Spectrum Disorder (ASD), asthma, nausea/vomiting and myopia. Acupuncture is not effective for epilepsy. Only six reviews reported adverse events (AEs) and no fatal side effects were reported.

CONCLUSION: The efficacy of acupuncture for some diseases is promising and there have been no fatal side effects reported. Further high quality studies are justified, with five diseases in particular as research priorities.

.....

Pediatrics. 2015 May;135:e1210-e1219.

VALIDITY OF THE STRENGTHS AND DIFFICULTIES QUESTIONNAIRE IN PRESCHOOL-AGED CHILDREN.

Croft S, Stride C, Maughan B, et al.

BACKGROUND: The Strengths and Difficulties Questionnaire (SDQ) is widely used to screen for child mental health problems and measure common forms of psychopathology in 4- to 16-year-olds. Using longitudinal data, we examined the validity of a version adapted for 3- to 4-year-olds.

METHODS: We used SDQ data from 16 659 families collected by the Millennium Cohort Study, which charts the development of children born throughout the United Kingdom during 2000-2001. Parents completed the preschool SDQ when children were aged 3 and the standard SDQ at ages 5 and 7. The SDQ's internal factor structure was assessed by using confirmatory factor analysis, with a series of competing models and extensions used to determine construct, convergent, and discriminant validity and measurement invariance over time. Predictive validity was evaluated by examining the relationships of age 3 SDQ scores with age 5 diagnostic measures of attention-deficit/hyperactivity disorder, autism spectrum disorder/Asperger syndrome, and teacher-reported measures of personal, social, and emotional development.

RESULTS: Confirmatory factor analysis supported a 5-factor measurement model. Internal reliability of subscales ranged from omega = 0.66 (peer problems) to omega = 0.83 (hyperactivity). Item-factor structures revealed measurement invariance over time. Strong positive correlations between ages 3 and 5 SDQ scores were not significantly different from correlations between age 5 and 7 scores. Conduct problems and hyperactivity subscales independently predicted developmental and clinical outcomes 2 years later.

CONCLUSIONS: Satisfactory psychometric properties of the adapted preschool version affirm its utility as a screening tool to identify 3- to 4-year-olds with emotional and behavioral difficulties.

.....

Pharmacoeconomics. 2015 May;33:489-509.

PROBABILISTIC MARKOV MODEL ESTIMATING COST EFFECTIVENESS OF METHYLPHENIDATE OSMOTIC-RELEASE ORAL SYSTEM VERSUS IMMEDIATE-RELEASE METHYLPHENIDATE IN CHILDREN AND ADOLESCENTS: WHICH INFORMATION IS NEEDED?

Schawo S, Van Der Kolk A, Bouwmans C, et al.

BACKGROUND: Incidence of attention deficit hyperactivity disorder (ADHD) in children and adolescents has been increasing. The disorder results in high societal costs. Policymakers increasingly use health economic evaluations to inform decisions on competing treatments of ADHD. Yet, health economic evaluations of first-choice medication of ADHD in children and adolescents are scarce and generally do not include broader societal effects.

OBJECTIVES: This study presents a probabilistic model and analysis of methylphenidate osmotic-release oral system (OROS) versus methylphenidate immediate-release (IR). We investigate and include relevant societal aspects in the analysis so as to provide cost-effectiveness estimates based on a broad societal perspective.

METHODS: We enhanced an existing Markov model and determined the cost effectiveness of OROS versus IR for children and adolescents responding suboptimally to treatment with IR. Enhancements included screening of a broad literature base, updated utility values, inclusion of costs and effects on caregivers and a change of the model type from deterministic to probabilistic.

RESULTS: The base case scenario resulted in lower incremental costs (<euro>-5815) of OROS compared with IR and higher incremental quality-adjusted life-year (QALY) gains (0.22). Scenario analyses were performed to determine sensitivity to changes in transition rates, utility of caregivers, medical costs of caregivers and daily medication dose.

CONCLUSIONS: The results indicate that, for children responding suboptimally to treatment with IR, the beneficial effect of OROS on compliance may be worth the additional costs of medication. The presented model adds to the health economic information available for policymakers and to considerations on a broader perspective in cost-effectiveness analyses.

.....

PLoS ONE. 2015;10:e0127237.

COST-EFFECTIVENESS OF EXTENDED-RELEASE METHYLPHENIDATE IN CHILDREN AND ADOLESCENTS WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER SUB-OPTIMALLY TREATED WITH IMMEDIATE RELEASE METHYLPHENIDATE.

van der Schans J, Kotsopoulos N, Hoekstra PJ, et al.

BACKGROUND: Attention-Deficit/Hyperactivity Disorder (ADHD) is a common psychiatric disorder in children and adolescents. Immediate-release methylphenidate (IR-MPH) is the medical treatment of first choice. The necessity to use several IR-MPH tablets per day and associated potential social stigma at school often leads to reduced compliance, sub-optimal treatment, and therefore economic loss. Replacement of IR-MPH with a single-dose extended release (ER-MPH) formulation may improve drug response and economic efficiency.

OBJECTIVE: To evaluate the cost-effectiveness from a societal perspective of a switch from IR-MPH to ER-MPH in patients who are sub-optimally treated.

METHODS: A daily Markov-cycle model covering a time-span of 10 years was developed including four different health states: (1) optimal response, (2) sub-optimal response, (3) discontinued treatment, and (4) natural remission. ER-MPH options included methylphenidate osmotic release oral system (MPH-OROS) and Equasym XL/Medikinet CR. Both direct costs and indirect costs were included in the analysis, and effects were expressed as quality-adjusted life years (QALYs). Univariate, multivariate as well as probabilistic sensitivity analysis were conducted and the main outcomes were incremental cost-effectiveness ratios.

RESULTS: Switching sub-optimally treated patients from IR-MPH to MPH-OROS or Equasym XL/Medikinet CR led to per-patient cost-savings of euro4200 and euro5400, respectively, over a 10-year treatment span. Sensitivity analysis with plausible variations of input parameters resulted in cost-savings in the vast majority of estimations.

CONCLUSIONS: This study lends economic support to switching patients with ADHD with suboptimal response to short-acting IR-MPH to long-acting ER-MPH regimens

.....

PLoS ONE. 2015;10:e0125573.

GAP EFFECT ABNORMALITIES DURING A VISUALLY GUIDED PRO-SACCADE TASK IN CHILDREN WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER.

Matsuo Y, Watanabe M, Taniike M, et al.

Attention deficit hyperactivity disorder (ADHD) is a neurodevelopmental disorder that starts in early childhood and has a comprehensive impact on psychosocial activity and education as well as general health across the lifespan. Despite its prevalence, the current diagnostic criteria for ADHD are debated. Saccadic eye movements are easy to quantify and may be a quantitative biomarker for a wide variety of neurological and psychiatric disorders, including ADHD. The goal of this study was to examine whether children with ADHD exhibit abnormalities during a visually guided pro-saccadic eye-movement and to clarify the neurophysiological mechanisms associated with their behavioral impairments. Thirty-seven children with ADHD (aged 5-11 years) and 88 typically developing (TD) children (aged 5-11 years) were asked to perform a simple saccadic eye-movement task in which step and gap conditions were randomly

interleaved. We evaluated the gap effect, which is the difference in the reaction time between the two conditions. Children with ADHD had a significantly longer reaction time than TD children (p < 0.01) and the gap effect was markedly attenuated (p < 0.01). These results suggest that the measurement of saccadic eye movements may provide a novel method for evaluating the behavioral symptoms and clinical features of ADHD, and that the gap effect is a potential biomarker for the diagnosis of ADHD in early childhood.

.....

PLoS ONE. 2015;10.

A LONGITUDINAL TWIN STUDY OF THE DIRECTION OF EFFECTS BETWEEN ADHD SYMPTOMS AND IQ. Rommel AS, Rijsdijk F, Greven CU, et al.

While the negative association between ADHD symptoms and IQ is well documented, our knowledge about the direction and aetiology of this association is limited. Here, we examine the association of ADHD symptoms with verbal and performance IQ longitudinally in a population-based sample of twins. In a population-based sample of 4,771 twin pairs, DSM-IV ADHD symptoms were obtained from the Conners ' Parent Rating Scale-Revised. Verbal (vocabulary) and performance (Raven's Progressive Matrices) IQ were assessed online. ADHD symptom ratings and IQ scores were obtained at ages 12, 14 and 16 years. Making use of the genetic sensitivity and time-ordered nature of our data, we use a cross-lagged model to examine the direction of effects, while modelling the aetiologies of the association between ADHD symptoms with vocabulary and Raven's scores over time. Although time-specific aetiological influences emerged for each trait at ages 14 and 16 years, the aetiological factors involved in the association between ADHD symptoms and IQ were stable over time. ADHD symptoms and IQ scores significantly predicted each other over time. ADHD symptoms at age 12 years were a significantly stronger predictor of vocabulary and Raven's scores at age 14 years than vice versa, whereas no differential predictive effects emerged from age 14 to 16 years. The results suggest that ADHD symptoms may put adolescents at risk for decreased IQ scores. Persistent genetic influences seem to underlie the association of ADHD symptoms and IQ over time. Early intervention is likely to be key to reducing ADHD symptoms and the associated risk for lower IQ.

.....

PLoS ONE. 2015;10:e0128325.

ANALYSIS OF PERSONAL AND FAMILY FACTORS IN THE PERSISTENCE OF ATTENTION DEFICIT HYPERACTIVITY DISORDER: RESULTS OF A PROSPECTIVE FOLLOW-UP STUDY IN CHILDHOOD.

Miranda A, Colomer C, Fernandez MI, et al.

OBJECTIVES: To study the course of ADHD during childhood and analyze possible personal and family predictor variables of the results.

METHOD: Sixty-one children with ADHD who were between 6 and 12 years old at the baseline assessment were evaluated 30 months later (mean age at baseline: 8.70 +/- 1.97; mean age at follow-up: 10.98 +/- 2.19). Status of ADHD in follow-up was identified as persistent (met DSM-IV-TR criteria according to parents' and teachers' ratings), contextually persistent (met ADHD criteria according to one informant, and there was functional impairment) and remitted ADHD (with subthreshold clinical symptomatology). Associated psychological disorders of the three groups were analyzed in the follow-up with the Conners' Rating Scales. The groups were compared on ADHD characteristics (symptoms of ADHD and impairment), child psychopathology, executive functioning (EF; inhibition, working memory) and parenting characteristics (parental stress and discipline styles) at baseline.

RESULTS: At the follow-up, 55.7% of the children continued to meet the DSM-IV-TR criteria for ADHD, 29.5% showed contextual persistence, and 14.8% presented remission of the disorder. The persistent and contextually persistent ADHD groups showed more associated psychological disorders. Inattention, oppositional problems, cognitive problems and impairment at baseline distinguished the remitted ADHD children from the persistent and contextually persistent ADHD children. Moreover, the persistent groups had significantly more emotional liability and higher parental stress than the group in remission, while no differences in EF where found among the groups.

CONCLUSIONS: ADHD children continue to present symptoms, as well as comorbid psychological problems, during adolescence and early adulthood. These findings confirm that persistence of ADHD is associated with child psychopathology, parental stress and impairment in childhood.

.....

Psychiatr Serv. 2015 Jun;66:617-24.

AN OBSERVATIONAL STUDY OF PHARMACOLOGICAL TREATMENT IN PRIMARY CARE OF CHILDREN WITH ADHD IN THE UNITED KINGDOM.

Raman SR, Marshall SW, Gaynes BN, et al.

OBJECTIVE: The study described initial pharmacological treatment of children in the United Kingdom diagnosed as having ADHD and assessed predictors of medication persistence.

METHODS: U.K. children ages 3-16 diagnosed as having ADHD between 1994 and 2006 were identified from primary care practice data. Child characteristics, prescription patterns, and initial medication prescribed were described over the study period. The associations of child and clinical factors with medication persistence (defined as initial treatment length greater than six months) were estimated by using binomial regression.

RESULTS: Of 2,878 children with an ADHD diagnosis, 46% (N=1,314) received at least one prescription for ADHD medication within two years of diagnosis. The mean initial treatment length was 10.7+/-.5 months. Only 35% (N=464) of pharmacologically treated children had a treatment length greater than six months after initial medication prescription when the analysis used a 30-day grace period; 57% were persistent in treatment when a less stringent 60-day grace period was used. Children who were initially prescribed long-acting methylphenidate were more likely to persist in treatment than those prescribed standard methylphenidate (risk ratio=1.2, 95% confidence interval=1.1-1.4).

CONCLUSIONS: A large proportion of children who received medication for ADHD in primary care did not continue in initial treatment for more than six months. Few child or clinical factors were associated with treatment persistence. Epidemiological research about the effects of long-term ADHD medication use should account for the observed limited persistence in medication treatment.

.....

Psychiatry Res. 2015 May.

INDIVIDUAL DIFFERENCES IN SUBCORTICAL MICROSTRUCTURE ORGANIZATION REFLECT REACTION TIME PERFORMANCES DURING A FLANKER TASK: A DIFFUSION TENSOR IMAGING STUDY IN CHILDREN WITH AND WITHOUT ADHD.

Fall S, Querne L, Le Moing AG, et al.

The results of several previous magnetic resonance imaging studies suggest that the fronto-striato-thalamic circuitry is involved in the pathophysiology of attention-deficit/hyperactivity disorder (ADHD). However, few studies have investigated the putative association between quantitative diffusion tensor imaging measurements of subcortical gray matter and subject task performances in children with ADHD. Here, we examined whether reaction time (RT) parameters during a flanker task were correlated with mean diffusivity (MD) measurements in the basal ganglia and thalamus in children with ADHD and in controls. For the study group as a whole, both the mean RT and the intra-individual variability in RTs were found to be significantly correlated with MD measurements in the right and left caudate, putamen and thalamus. In contrast, the correlation between the interference effect and MD failed to reach statistical significance. The present results may advance our understanding of the anatomical substrates of ADHD.

Psychiatry Res. 2015 Jul;228:77-82.

NEUROLOGICAL SOFT SIGNS IN CHILDREN WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER: THEIR RELATIONSHIP TO EXECUTIVE FUNCTION AND PARENTAL NEUROLOGICAL SOFT SIGNS.

Gong J, Xie J, Chen G, et al.

The correlations between neurological soft signs (NSS) in children with attention deficit hyperactivity disorder (ADHD) and their executive function, symptoms of inattention, and hyperactivity-impulsivity and the NSS of their parents remain unclear. This study aimed to examine: (1) the prevalence of NSS in children with ADHD and their parents; (2) the correlation between the NSS of children with ADHD and their executive function between the NSS of children with ADHD and their executive function and symptoms. NSS were assessed with the Cambridge Neurological Inventory (CNI) in 57 children with ADHD (and 80 parents) and 60 healthy children (and 75 parents). Executive function was measured with the Behavioral Rating Inventory of Executive Function (BRIEF). Children with ADHD and their parents had significantly higher NSS than normal children and their parents, respectively, and the NSS of children with ADHD were correlated more strongly with the NSS of their fathers than their mothers. No correlation was found between NSS and BRIEF executive function, but Disinhibition in children with ADHD was significantly correlated with hyperactivity-impulsivity symptoms. Paternal and maternal NSS provided different predictions for child NSS. It may be that NSS are more likely to be genetically transmitted by fathers.

.....

Psychol Med. 2015 Jun;45:1601-12.

ASSOCIATION BETWEEN PHTHALATES AND EXTERNALIZING BEHAVIORS AND CORTICAL THICKNESS IN CHILDREN WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER.

Park S, Lee JM, Kim JW, et al.

BACKGROUND: Previous studies have implicated the relationship between environmental phthalate exposure and attention deficit hyperactivity disorder (ADHD) symptoms of childhood, but no studies have been conducted in children who have a confirmed diagnosis of ADHD obtained through meticulous diagnostic testing. We aimed to determine whether phthalate metabolites in urine would be higher in children with ADHD than in those without ADHD and would correlate with symptom severity and cortical thickness in ADHD children.

METHOD: A cross-sectional examination of urine phthalate metabolite concentrations was performed; scores for ADHD symptoms, externalizing problems, and continuous performance tests were obtained from 180 children with ADHD, and brain-imaging data were obtained from 115 participants. For the control group, children without ADHD (N = 438) were recruited. Correlations between phthalate metabolite concentrations and clinical measures and brain cortical thickness were investigated.

RESULTS: Concentrations of phthalate metabolites, particularly the di(2-ethylhexyl) phthalate (DEHP) metabolite, were significantly higher in boys with ADHD than in boys without ADHD. Concentrations of the di-n-butyl phthalate (DBP) metabolite were significantly higher in the combined or hyperactive-impulsive subtypes compared to the inattentive subtype, and the metabolite was positively correlated with the severity of externalizing symptoms. Concentrations of the DEHP metabolite were negatively correlated with cortical thickness in the right middle and superior temporal gyri.

CONCLUSIONS: The results of this study suggest an association between phthalate concentrations and both the diagnosis and symptom severity of ADHD. Imaging findings suggest a negative impact of phthalates on regional cortical maturation in children with ADHD.

Psychol Med. 2015 May;1-9.

ASSOCIATIONS BETWEEN SEROTONIN TRANSPORTER GENE (SLC6A4) METHYLATION AND CLINICAL CHARACTERISTICS AND CORTICAL THICKNESS IN CHILDREN WITH ADHD.

Park S, Lee JM, Kim JW, et al.

BACKGROUND: Attention deficit hyperactivity disorder (ADHD) is a common, highly heritable psychiatric disorder. Additionally, environmental factors such as perinatal stress and early adversities contribute to the occurrence and severity of ADHD. Recently, DNA methylation has emerged as a mechanism that potentially mediates gene-environmental interaction effects in the aetiology and phenomenology of psychiatric disorders. Here, we investigated whether serotonin transporter gene (SLC6A4) methylation patterns were associated with clinical characteristics and regional cortical thickness in children with ADHD. **METHOD**: In 102 children with ADHD (age 6-15 years), the methylation status of the SLC6A4 promoter was measured. Brain magnetic resonance imaging was obtained and ADHD symptoms were evaluated.

RESULTS: A higher methylation status of the SLC6A4 promoter was significantly associated with worse clinical presentations (more hyperactive-impulsive symptoms and more commission errors). Additionally, a negative correlation was observed between SLC6A4 methylation levels and cortical thickness values in the right occipito-temproral regions.

CONCLUSIONS: Our results suggest that the SLC6A4 methylation status may be associated with certain symptoms of ADHD, such as behavioural disinhibition, and related brain changes. Future studies that use a larger sample size and a control group are required to corroborate these results.

.....

Psychol Rep. 2015 Jun.

MATERNAL RATINGS OF BULLYING AND VICTIMIZATION: DIFFERENCES IN FREQUENCIES BETWEEN PSYCHIATRIC DIAGNOSES IN A LARGE SAMPLE OF CHILDRE.

Mayes SD, Calhoun SL, Baweja R, et al.

-Little is known about psychiatric diagnoses that place children at risk for bullying and victimization. Mothers of 1,707 children 6-18 yr. rated their child as a bully and a victim (not at all, to very often a problem) on the Pediatric Behavior Scale. Children with psychiatric diagnoses were evaluated in an outpatient psychiatry clinic (M age = 9.2 yr., 68.4% male). Control children were community children not on psychotropic medication and with no neurodevelopmental disorder (M age = 8.7 yr., 43.5% male). Children with autism, intellectual disability, and ADHD-Combined type had higher victim and bully maternal ratings than children in the ADHD-Inattentive, depression, anxiety, eating disorder, and control groups. Eating disorder and controls were the only groups in which most children were not rated a victim or a bully. Comorbid oppositional defiant disorder accounted for the higher bully ratings for ADHD-Combined, autism, and intellectual disability. Victimization ratings did not differ between psychiatric groups. Except for eating disorders, victimization ratings were greater in all groups than in control children, suggesting that most psychiatric disorders place children at risk for victimization, as perceived by their mothers.

.....

Psychol Assess. 2015.

FACTOR STRUCTURE OF SYMPTOM DIMENSIONS IN ATTENTION-DEFICIT/HYPERACTIVITY DISORDER (ADHD). Parke EM, Mayfield AR, Barchard KA, et al.

There is disagreement on whether attention-deficit/hyperactivity disorder (ADHD) symptoms are best characterized along two dimensions consisting of inattention and hyperactivity/impulsivity or three dimensions where hyperactivity and impulsivity are separate. To address this, the current study investigated the underlying symptom dimensions of ADHD by examining two- and three-factor models of ADHD symptom ratings in 400 children and adolescents diagnosed with ADHD. ADHD symptom ratings for each of the 18 DSM-IV Criteria A symptoms were obtained from mothers using a standardized symptom rating scale. Confirmatory factor analysis (CFA) was used to examine whether the 18 symptoms were best explained by two or three latent constructs. Results of the CFA demonstrated that a three-factor model was superior to a two-factor model. Findings support three distinct symptom dimensions that are consistent with

previous research demonstrating unique clinical presentations of inattention, hyperactivity, and impulsivity. Differentiating between these three domains may aid in predicting behavioral outcomes in children with ADHD.

.....

Regul Toxicol Pharmacol. 2015;72:244-48. REGULATORY ACTION AND MODERATE DECREASE IN METHYLPHENIDATE USE AMONG ADHD DIAGNOSED PATIENTS AGED FIVE AND UNDER IN KOREA.

Shin J-Y, Lee SH, Shin SM, et al.

In December 2009, Korean regulatory agency announced that methylphenidate, a drug used to treat attention deficit-hyperactivity disorder (ADHD), should not be used in children aged five and under due to the risk of sudden cardiac death. This study examined the impact of regulatory action and prescribing patterns. We conducted a time series analysis using the Korea National Health Insurance Service database. Study subjects included children under 18. years old with ADHD from January 2007 to December 2011. Contraindicated use of methylphenidate was defined as use of methylphenidate at least once in children aged five and under. We selected additional control points (2007, 2008, and 2010) and compared the methylphenidate use one year before and after each point. We calculated relative and absolute reductions, and 95% confidence intervals. The total number of ADHD patients was 376,298. Overall, there was a 70.87% relative reduction (95% CI: 63.33%-79.31%) and a 0.93% absolute reduction (95% CI: 0.51%-0.60%) of methylphenidate use. The relative and absolute reductions were 27.61% (95% Cl: 24.76%-30.78%) and 0.31% (95% Cl: 0.21%-0.41%) in 2007; 43.58% (95% Cl: 38.02%-49.96%) and 0.35% (95% CI: 0.27%-0.43%) in 2008; 46.52% (95% CI: 38.86%-55.70%) and 0.21 (95% CI: 0.15%-0.27%) in 2009; and 10.20% (95% CI: 8.32%-12.50%) and 0.02% (95% CI: 0.02%-0.07%) in 2010. Korean regulatory action led to a moderate decrease in contraindicated methylphenidate use even after the steep decline before the regulatory action.

.....

Rev Bras Psiquiatr. 2015 May;0.

ATTENTIONAL BLINK IN CHILDREN WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER.

Amador-Campos JA, Aznar-Casanova JA, Bezerra I, et al.

OBJECTIVE: To explore the temporal mechanism of attention in children with attention deficit hyperactivity disorder (ADHD) and controls using a rapid serial visual presentation (RSVP) task in which two letters (T1 and T2) were presented in close temporal proximity among distractors (attentional blink [AB]).

METHOD: Thirty children aged between 9 and 13 years (12 with ADHD combined type and 18 controls) took part in the study. Both groups performed two kinds of RSVP task. In the single task, participants simply had to identify a target letter (T1), whereas in the dual task, they had to identify a target letter (T1) and a probe letter (T2).

RESULTS: The ADHD and control groups were equivalent in their single-task performance. However, in the dual-task condition, there were significant between-group differences in the rate of detection of the probe letter (T2) at lag + 1 and lag + 4. The ADHD group exhibited a larger overall AB compared with controls.

CONCLUSION: Our findings provide support for a link between ADHD and attentional blink.

.....

Sleep. 2015;38:A20.

NOVEL ACTIGRAPHIC MEASURES DEMONSTRATE GREATER SLEEP DISTURBANCE IN YOUNG CHILDREN WITH SYMPTOMS OF ADHD.

Desrochers P, Cremone A, Peterson B, et al.

Introduction: Sleep disturbances are prevalent in children with Attention Deficit Hyperactivity Disorder (ADHD) and are thought to precede the onset of symptoms. However, as yet, evidence of sleep deficits

prior to or at the time of diagnosis is scarce and inconsistent. To this end, we used actigraphy and polysomnography (PSG) to examine sleep in young children with (ADHD group) and without (control group) symptoms of ADHD.

Methods: Recruited children were assessed with the DSM-IV by a trained clinician. Those with (greaterthan or equal to) 6 symptoms of ADHD were included in the ADHD group (n = 8, M = 80 months) while those with < 4 symptoms were included in the control group (n = 7; M = 85 months). Actigraphy was recorded for 3-10 days (M = 7 days). Additionally, 1-night of overnight PSG was collected.

Results: Contrary to results from studies in older children with diagnosed ADHD, PSG architecture was not statistically different between groups, including Wake After Sleep Onset (WASO; t(10) = -1.251, p = 0.244). Actigraphic estimates of aWASO showed that it was greater in the ADHD group but the difference was not statistically significant (p = 0.08). However, analysis of the motion data collected by actigraphy showed that the ADHD group had a larger mean activity during the night (16.2 (plus or minus) 5.2 vs 11.7 (plus or minus) 1.5 cts/min, p < 0.05) and a larger 95th percentile activity level (p < 0.05). In addition, the activity pattern of the ADHD group had a different distribution of activity values as evidenced by differences in skewness (p < 0.02) and kurtosis (p < 0.03).

Conclusion: These data demonstrate an additional information may be obtained from actigraphy data by analyzing motion patterns. This information may detect an early difference in sleep of children with and without ADHD symptoms, which may help identify children who are at-risk for developing ADHD, creating opportunities for earlier diagnosis and intervention.

.....

Sleep. 2015;38:A12.

SLEEP SPINDLE-FREQUENCY EEG ACTIVITY IS ASSOCIATED WITH OVERNIGHT MOTOR SKILL IMPROVEMENT IN CHILDREN WITH ATTENTION-DEFICIT-HYPERACTIVITY-DISORDER.

Saletin JM, Coon WG, Carskadon MA.

Introduction: Pediatric attention-deficit-hyperactivity-disorder (ADHD) is associated with motor learning deficits and sleep abnormalities. In adults, Stage 2 sleep spindles predict improvements in motor learning following sleep. This association is poorly characterized in children, and particularly in pediatric ADHD.

Methods: Following a standardized at-home stabilization period and an in-lab adaptation night, Polysomnographic sleep was monitored (~10 hr) in seven children with ADHD (2F, 11.9 (plus or minus) 0.9 years, abstaining from medication; ADHD-status confirmed from diagnostic interviews) and 14 typicallydeveloping controls (4F, 11.7 (plus or minus) 0.9 years). All children trained on a validated motor sequence task (MST) in the evening (~1 hr prior to bed) with retesting the following morning (~1 hr after awakening); analyses focused on MST accuracy (correct sequences as a proportion of all keystrokes). Performance was summarized in the evening as the average of the final two learning trials and in the morning as the average of the first two learning trials.

Results: Mixed-effects models confirmed a main-effect of sleep; MST accuracy improved overnight (Wald-(chi)2 = 17.56, p < 0.001). A significant condition-x-group interaction (Wald-(chi)2 = 6.08, p = 0.014), however, indicated that accuracy improved overnight in children with ADHD (Wald-(chi)2 = 16.61, p < 0.001) but not in controls (Wald-(chi)2 = 2.23, p = 0.135). Although evening accuracy was lower in ADHD (Wald-(chi)2 = 3.90, p = 0.048), morning accuracy did not differ between groups (Wald-(chi)2 = 2.23, p = 0.135), suggesting an overnight normalization of performance. Stage 2 EEG power spectra were examined to explore a possible mechanism underlying this skill improvement. ADHD-status moderated the association between slow spindle activity (12-13.5 Hz) and overnight accuracy improvement ((beta) = 1.289, p = 0.023); furthermore, spindle-frequency EEG activity positively predicted improvements in ADHD ((beta) = 0.792, p = 0.021) but not in controls ((beta) = 0.056, p = 0.817).

Conclusion: These data indicate that motor skill learning in children with ADHD, as shown in adults, benefits from sleep, particularly sleep spindle EEG frequencies. Sleep disturbance in ADHD, therefore, may in part underlie cognitive deficits commonly observed in this population.

Soc Psychiatry Psychiatr Epidemiol. 2015 May.

IS THE PREVALENCE OF ADHD IN TURKISH ELEMENTARY SCHOOL CHILDREN REALLY HIGH? Ercan ES, Bilac O, Uysal OT, et al.

PURPOSE: Previous findings in Turkish samples of children have suggested higher prevalence of ADHD than those detected in Western cultures. Methodological problems might explain these findings. Here, we aimed to re-check the prevalence rate of Attention-Deficit/Hyperactivity Disorder (ADHD) along with other childhood psychiatric disorders in a representative school sample of elementary school children in Izmir, Turkey.

METHOD: The sample consisted of 419 randomly selected primary school children aged 6-14-year-old. We were able to interview 417 cases (99.5 % of the sample). Psychiatric diagnoses in children were assessed using the K-SADS-PL (Schedule for Affective Disorders and Schizophrenia for School-Age Children-Present and Lifetime Version) and an impairment criterion scale.

RESULTS: The prevalence rates of ADHD were 21.8 and 12.7 % in children without and with impairment, respectively. The following major mental disorders were significantly more prevalent in ADHD cases than controls: oppositional defiant disorder (ODD) (9.4 versus 0 %), conduct disorder (15.1 versus 0 %), anxiety (17 versus 0.5 %), and mood (5.7 versus 0.8 %).

CONCLUSIONS: Our results confirmed a substantially higher ADHD prevalence rate (more than double) than the suggested pooled worldwide prevalence, although similar to the one recently detected in a representative populational sample of children in the US (11 %). These findings, consistent with previous developmental epidemiology studies from Turkey, confirm that ADHD is highly prevalent in Turkish elementary school children.

.....

Telemed J E Health. 2015 Jun;21:451-58.

TELETHERAPY DELIVERY OF CAREGIVER BEHAVIOR TRAINING FOR CHILDREN WITH ATTENTION-DEFICIT HYPERACTIVITY DISORDER.

Tse YJ, McCarty CA, Stoep AV, et al.

BACKGROUND: Preliminary studies suggest that videoteleconferencing (VTC) may be an effective means to deliver behavioral interventions to families. Subjects consisted of a subsample of children (n=37) and caregivers who participated in the Children's Attention-Deficit Hyperactivity Disorder (ADHD) Telemental Health Treatment Study (CATTS) (n=223), a randomized trial testing the effectiveness of delivering treatments for ADHD to families residing in their home communities using distant technologies. Families randomized to the CATTS intervention arm received pharmacotherapy and caregiver behavior training.

MATERIALS AND METHODS: Thirty-seven families from the CATTS intervention arm participated. All families received pharmacotherapy through VTC. Twelve families received the caregiver behavior training through VTC, or teletherapy, and 25 received the intervention in-person. We assessed children's outcomes at 25 weeks with the Vanderbilt ADHD Parent Rating Scale and the Columbia Impairment Scale. We assessed caregivers' outcomes using measures of distress in caring for a child with ADHD, including depression, stress, strain, and empowerment. We used analysis of covariance to assess outcomes from baseline to 25 weeks.

RESULTS: Families in the two conditions showed comparable attendance at sessions and satisfaction with their care. Caregivers in both conditions reported comparable outcomes for their children's ADHD-related behaviors and functioning, but caregivers in the teletherapy group did not report improvement in their own distress.

CONCLUSIONS: Findings support the feasibility, acceptability, and effectiveness of treating children with ADHD through teletherapy. Future work should investigate how teletherapy may improve caregivers' distress. Teletherapy is a promising modality for delivering behavioral interventions for children with ADHD.

Transl Psychiatry. 2015;5.

THE RELATIVE CONTRIBUTION OF COMMON AND RARE GENETIC VARIANTS TO ADHD.

Martin J, O'Donovan MC, Thapar A, et al.

Attention deficit hyperactivity disorder (ADHD) is highly heritable. Genome-wide molecular studies show an increased burden of large, rare copy-number variants (CNVs) in children with ADHD compared with controls. Recent polygenic risk score analyses have also shown that en masse common variants are enriched in ADHD cases compared with population controls. The relationship between these common and rare variants has yet to be explored. In this study, we tested whether children with ADHD with (N = 60) a large (4500 kb), rare (o1% frequency) CNV differ by polygenic risk scores for ADHD to children with ADHD with a group of population controls (N = 4670; of whom N = 397 had CNVs). The results show that children with ADHD with large, rare CNVs have lower polygenic scores than children without such CNVs (odds ratio (OR) = 0.73, P = 0.023). Although ADHD children without CNVs had higher scores than controls (OR = 1.18, P = 0.0031), this difference was not observed for ADHD children with CNVs (OR = 0.86, P = 0.27). These results are consistent with a polygenic liability threshold model of ADHD with both common and rare variants involved.

.....

Trials. 2015.

NEUROFEEDBACK AS A NONPHARMACOLOGICAL TREATMENT FOR ADULTS WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER (ADHD): STUDY PROTOCOL FOR A RANDOMIZED CONTROLLED TRIAL. *Mayer K, Wyckoff SN, Fallgatter AJ, et al.*

Background: Neurofeedback has been applied effectively in various areas, especially in the treatment of children with attention-deficit/hyperactivity disorder (ADHD). This study protocol is designed to investigate the effect of slow cortical potential (SCP) feedback and a new form of neurofeedback using near-infrared spectroscopy (NIRS) on symptomatology and neurophysiological parameters in an adult ADHD population. A comparison of SCP and NIRS feedback therapy methods has not been previously conducted and may yield valuable findings about alternative treatments for adult ADHD.

Methods/Design: The outcome of both neurofeedback techniques will be assessed over 30 treatment sessions and after a 6-month follow-up period, and then will be compared to a nonspecific biofeedback treatment. Furthermore, to investigate if treatment effects in this proof-of-principle study can be predicted by specific neurophysiological baseline parameters, regression models will be applied. Finally, a comparison with healthy controls will be conducted to evaluate deviant pretraining neurophysiological parameters, stability of assessment measures, and treatment outcome.

Discussion: To date, an investigation and comparison of SCP and NIRS feedback training to an active control has not been conducted; therefore, we hope to gain valuable insights in effects and differences of these types of treatment for ADHD in adults.

Trial registration: This study is registered with the German Registry of Clinical Trials: DRKS00006767, date of registration: 8 October 2014.

.....

Twin Res Hum Genet. 2015;18:171-78.

SHARED GENETIC AND ENVIRONMENTAL INFLUENCES ON EARLY TEMPERAMENT AND PRESCHOOL PSYCHIATRIC DISORDERS IN HISPANIC TWINS.

Silberg JL, Gillespie N, Moore AA, et al.

Objective: Despite an increasing recognition that psychiatric disorders can be diagnosed as early as preschool, little is known how early genetic and environmental risk factors contribute to the development of psychiatric disorders during this very early period of development.

Method: We assessed infant temperament at age 1, and attention deficit hyperactivity disorder (ADHD), oppositional defiant disorder (ODD), and separation anxiety disorder (SAD) at ages 3 through 5 years in a sample of Hispanic twins. Genetic, shared, and non-shared environmental effects were estimated for each

temperamental construct and psychiatric disorder using the statistical program MX. Multivariate genetic models were fitted to determine whether the same or different sets of genes and environments account for the co-occurrence between early temperament and preschool psychiatric disorders.

Results: Additive genetic factors accounted for 61% of the variance in ADHD, 21% in ODD, and 28% in SAD. Shared environmental factors accounted for 34% of the variance in ODD and 15% of SAD. The genetic influence on difficult temperament was significantly associated with preschool ADHD, SAD, and ODD. The association between ODD and SAD was due to both genetic and family environmental factors. The temperamental trait of resistance to control was entirely accounted for by the shared family environment.

Conclusions: There are different genetic and family environmental pathways between infant temperament and psychiatric diagnoses in this sample of Puerto Rican preschool age children.

.....

Zeitschrift für Kinder- und Jugendpsychiatrie und Psychotherapie. 2015 Mar;43:133-44.

KLINISCHE DIAGNOSTIK DER ADHS IM VORSCHULALTER. = CLINICAL DIAGNOSTICS OF ADHD IN PRESCHOOL-AGED CHILDREN.

Merkt J, Petermann F.

Attention deficit hyperactivity disorder (ADHD) is one of the most prevalent psychiatric disorders in childhood and adolescence and has many negative consequences for both the child and the family. Early identification of children with ADHD would be helpful for the prevention of long-term consequences. This review appraises questionnaires and clinical interviews that can be used for the diagnosis of ADHD in preschool-aged children (3–5 years). We compare and discuss both German and international methods. The role of questionnaires and clinical interviews in the diagnostic process of ADHD is discussed.

176

A Comparison between Children with ADHD and Children with Epilepsy in Self-Esteem and Parental Stress Level

Antonella Gagliano^{1,*,#}, Marco Lamberti^{1,2,*,#}, Rosamaria Siracusano¹, Massimo Ciuffo¹, Maria Boncoddo¹, Roberta Maggio¹, Simona Rosina¹, Clemente Cedro³ and Eva Germanò¹

¹Division of Child Neurology and Psychiatry, University of Messina, Italy; ²Department of Clinical and Experimental Medicine, University of Messina, Italy; ³Division of Psychiatry, University of Messina, Italy

Abstract: Attention-deficit/hyperactivity disorder (ADHD) is frequently associated with negative psychological outcomes. This study explores the relationship between self-esteem, ADHD symptoms and parental stress. It compares children with ADHD, children with epilepsy (E) and typical developmental controls (TD). Participants included 65 children (aged 9-12 yrs) and their parents. The assessment was conducted by Multidimensional Self-Concept Scale (MSCS), Parent Stress Index (PSI) and Conners' Parent Rating Scales–Revised. Significant differences were found in Social, Competence and Academic areas of self-esteem between children with ADHD, with E and TD. Moreover, parents of children with ADHD showed a higher overall stress than both other groups. In conclusion, it seems important to evaluate the psychological aspects of ADHD condition, both in children and in parents, in order to suggest an individual multimodal treatment.

Keywords: Attention-deficit/hyperactivity disorder, children, epilepsy, parental stress, self-esteem.

INTRODUCTION

Several syndromes and developmental disorders are commonly associated with low levels of self-esteem. Conversely, a low self-esteem may be a signal of distress associated with serious impairments in psychological development. Attention-deficit/hyperactivity disorder (ADHD), a common child and adolescent disorder, is frequently associated with low self-esteem and low self-perception, negative outcomes and emotional and behavioural problems [1, 2]. ADHD makes it difficult to achieve success and fulfillment at school [3], at home and during free time. Increasingly, the literature suggests that affected children are more likely to experience school failure, poor peer relationships, and familial conflict [4-6]. In particular, lower scores in sub-domains of selfesteem such as "skills and talents" and "psychological wellbeing" in children with high scores of ADHD symptoms have been reported [7]. On the whole, low self-esteem has been associated with feelings of inadequacy and frustration which in turn can result in the worsening of behavioural symptoms. Indeed, a poor self-concept related to academic competence can directly contribute to the development of disruptive, antisocial behaviors in early adolescence [8].

However, findings from previous studies investigating the relationship between Attention-deficit/hyperactivity disorder (ADHD) and self-esteem are inconsistent. Some studies indicate that self-esteem scores are lower in children with ADHD than typical developmental children (TD) [2, 8, 9], others report that self-esteem scores are higher in children with ADHD [10]. In particular elementary-age children with ADHD display overly positive self-perceptions, a condition described as a "positive illusory bias" (PIB) [11-13]. The PIB has been defined in the following way: "children with ADHD unexpectedly provide extremely positive reports of their own competence in comparison to other criteria reflecting actual competence" [14]. Current literature supporting the presence of the PIB in individuals with ADHD has been conducted primarily with elementary-age students. However, academic and social problems associated with ADHD may become more prominent during adolescence due to the increasing academic demands and the increased emphasis on peer acceptance [15]. Interestingly, self-concept seems to decrease with age in children with ADHD and those with internalizing problems are at greater risk for poor self-esteem [16]. ADHD adolescent's sense of self can also be affected by both the core symptoms and environmental factors, such as parental difficulty in managing their children [17]. Some authors, using twin methodology [18] have argued for the existence of a long-term relationship between ADHD symptoms reported by parents, measured at 8 years of age, and a self-report of low self-esteem measured at 13 years. They suggested that children with ADHD may experience heightened risk of developing clinically low self-esteem in early adolescence.

The current study examines the relationship between ADHD and self-esteem, and observes how self-esteem impacts on the relation between parental stress and ADHD symptoms. We hypothesized that children with ADHD have a self-esteem even lower than children with a chronic and severe condition as epilepsy. In fact, children with epilepsy do not always show lower self-esteem than their peers [19-21] and some studies indicate that children with physical

1745-0179/14 2014 Bentham Open

^{*}Address correspondence to this author at the Division of Child Neurology and Psychiatry, University of Messina, Italy;

E-mail: mlamberti@unime.it

[#]Joint first authors

impairments are not always impaired as regards their selfesteem [22]. However, epilepsy is commonly considered a very debilitating disease that could have a strong impact on self-esteem because of the clear perception of the illness, the need for long-term drug therapy, the social stigma attached to the illness and other resulting problems [23]. In a certain sense the characteristics of the epileptic condition could be considered very close to of ADHD characteristics. Moreover, parents of patients with epilepsy are directly involved in the management of children's condition just as the parents of children with ADHD. Taking into consideration these similarities, we decided to compare children with ADHD to children with epilepsy.

An additional goal of the current study was to determine the extent to which perceived parental stress is related to the management of children with ADHD symptoms. It is well known that parents of children with ADHD experience elevated levels of caregiver stress. Many studies have reported very high parent stress levels related to the severity of children's ADHD symptoms, aggression, emotional liability, and executive functioning difficulties [24]. Recent research has shown that the perceived impairments in children's selfregulation across emotional, cognitive, and behavioural domains are what parents report as stressful, not simply the severity of ADHD symptoms [25]. As a matter of fact, the link between child behaviours and maternal distress seems strengthened by maternal risk and attenuated by child behavioural self-esteem [26]. Thus, we planned to exam the correlation between child self-esteem and parental stress.

METHODS

Sample

Subjects attending our programs in the Unit of Child Neurology and Psychiatry of the University Clinic were considered for the study. The study was approved by the local Ethics Committee.

Participants included 65 children and their parents: 22 children with a diagnosis of ADHD (according to DSM-IV-TR criteria; 17 combined subtype and 5 inattentive subtype) aged 9-12 years (M = 10,14, SD = .990), 20 children with Epilepsy (Idiopathic epilepsy with partial or secondarily generalized seizures) aged 9-12 years (M = 10,85, SD = .813), and 23 typically developing children (TD) recruited in two different schools in Messina and examined within their school environment. The groups were comparable for gen-

der, age of patient and parents, level of education, number of siblings and socio-economic background. Demographic features are reported in Table 1.

We excluded subjects with low IQ (total IQ below 85 at WISC-III scale), specific learning disorders (such as dyslexia), major neurological signs and sensory deficits.

At the moment of evaluation, 10/22 patients with ADHD were on pharmacological treatment with stimulants, and 12/20 patients with epilepsy were on antiepileptic drugs (5 with acid valproic, 4 with carbamazepine, 3 with levetiracetam).

Measures

Multidimensional Self Concept Scale [27] SCS, Bracken, 1993; MTA Italian version Beatrice & Bracken,2005) was used to investigate the participants' global level of self-esteem.

MSCS is a self-report instrument, which consists of 150 items exploring six areas by six subscales: *Social, Competence, Affect, Academic, Family and Phisical.* MSCS subscales analyze some personal traits and social characteristics (see Table 2). The information about the person/individual in several domains of varying contexts is used to create multidimensional personal profiles [28]. Therefore, an individual value profile consists of the values in the variables constituting the profile, described by the subscales of the questionnaire. The multiple answering options are: *Absolutely True, True, False, Absolutely False.*

Parenting Stress Index [29] is used to measure parental stress level. This self-report instrument is aimed to explore the stress levels of parents or caregivers. It consists of 36 items that describe feelings and behaviours related to parental stress. Five answering options are proposed for each item: *Absolutely Agree* (AA), *Agree* (A),*Not Sure* (NS), *Disagree* (D), *Absolutely Disagree* (AD).

The instrument is based on the assumption that parental stress originates not only from characteristics of children and parents but also from socio-demographic features.

It analyzes three subscales:

- Parental Distress (PD)
- Parent-Child Dysfunctional Interaction (P-CDI)
- Difficult Child (DC)

Table 1. Demographic characteristics of children with Attention-Deficit/Hyperactivity Disorder (ADHD), epilepsy and typical developmental.

	AD Mea	OHD un SD	EPII Mea	LEPSY an SD	TD Mean SD		
Age children	10,14 ,990		10,85	,813	10,61	1,08	
Male	100%		10	00%	100%		
Siblings	1,14	1,16	1,33	,594	1,22	,671	
Age mother	40,4	3,95	41,20	5,1	42,39	5,0	
Age father	43,50	4,091	43,84	4,2	45,9	6,5	

p < 0,05 p < 0,01

Table 2.MSCS subscales.

Social subscale: social competence related to interactions with others;
Competence subscale: success/failure in attainment of goals:
Affect subscale: recognition if affective behaviors
<i>Academic subscale</i> : academic achievement and competence in other school-related activities:
Family subscale: competence related to interaction with family members
Physical subscale: physical attractiveness and prowess.

Conners' Parent Rating Scales–Revised, [30] is commonly used to quantify ADHD symptoms. We asked the parents to complete the Conners' Parents Rating Scales Revised, Short Form (CPRS-R:S, Conners, 1989). The CPRS-R:S contains 27 items and covers a subset of the subscales and items on the long parent form.

It provides the following sub-scores:

- Oppositional : probes like children are " predisposed " to break rules,
- Cognitive Problems/Inattention: probes like subject may experience learning difficulties, of difficulty in organizing school work,
- Hyperactivity : probes like subject finds it difficult to sit in the classroom or pay attention for a long-time,
- ADHD Index: probes to identify children / adolescents "at risk" of ADHD.

Statistical Analyses

Descriptive analyses were used to analyze demographic and clinical characteristics of the whole sample. Chi-square analyses were performed on categorical variables and unpaired t-test on continuous variables. Bonferroni multiple comparison method was performed to compare the test variables between each group. Effect size was calculated for relevant differences by Hedge method. Furthermore, correlation analyses were performed between variables for each group using Pearson's correlation coefficients.

RESULTS

Significant differences were found across the explored domains between children with ADHD, and typically developing children. Table **3** and Fig. (1) show the means and SD of the differences in MSCS domains between the three groups.

There are statistically significant differences in MSCS subscales between the ADHD group and TD group in the Social area (p, 004), in the Competence area (p, 008) and in the Academic area (p, 032). Even if the mean overall MSCS scores of children with ADHD is not greatly impaired, some subjects out of the whole group obtained very low scores, as shown in Fig. (2). Notably, patients with ADHD obtained higher scores in "Physical" subscale compared to the other two groups (see Fig. 2). Conversely, no statistical differences emerged between children with epilepsy and typically developing controls in any of the MSCS areas and between ADHD and children with epilepsy. In one out the MSCS subscales (*Family*) children with epilepsy showed a higher level of self-esteem than typically developing children.

Analysing the PSI scores, we observed that parents of children with ADHD had significantly higher scores than parents of typically developing children. Parent Stress Index (PSI) mean scores, analysed by Bonferroni multiple comparison for all parameters, between ADHD group, epilepsy group and TD group, were significantly different (see Table 4). ADHD group and TD group differ significantly in P-CDI (Parent-Child Dysfunctional Interaction, p,000), DC (Difficult Child, p,000) and PSI -TS (Parental stress index total score sub-scores, p,000) sub-scores.

But also the difference between Epilepsy group and ADHD group was statistically significant in P-CDI (Parent-Child Dysfunctional Interaction, p,018) and DC (Difficult Child, p,028) sub-scores. Therefore, parents of children with ADHD showed a higher overall stress than both the parents of TD and epilepsy groups (see Fig. 2).

Table 3.	Mean scores, SD and bonferroni multiple comparison method for all parameters of Multidimensional self concept scale
	(MSCS): comparison between children with attention-deficit/hyperactivity disorder (ADHD), epilepsy and typical devel-
	opmental. Effect size by g of hedge.

MSCS Domains	ADHD Mean SD		EPILEPSY Mean SD		TD Mean SD		P value A/E A/C E/C			Effect Size t
Social	91,7	12,0	100	13,8	104,1	11,5	,109	,004**	,847	>1
Competence	90,2	14,5	94,1	13,9	102,9	12,1	1	,008**	,115	>1
Affect	97,0	12,7	102,6	12,2	103,0	9,1	,356	,260	1	
Academic	93,1	14,3	102,4	15,2	103,6	10,0	,083	,032*	1	>1
Family	97,1	9,7	103,2	9,4	99,0	10,5	,153	1	,527	
Physical	105,1	12,1	102,1	14,8	103,6	10,5	1	1	1	
MSCS tot	95,4	11,4	101,6	10,5	102,5	10,6	,212	,094	1	

* p < 0,05 ** p < 0,01



Fig. (1). Comparison between the three groups in MSCS.



Fig. (2). Comparison between the three groups in PSI.

 Table 4.
 Mean scores, SD and bonferroni multiple comparison method for all parameters of parent stress index (PSI): comparison between Attention-Deficit/Hyperactivity Disorder (ADHD), epilepsy and typical developmental children's parents.

PSI Domains	AD Mea	HD n SD	EPIL Mea	EPSY in SD	T Mea	D n SD	P value A/E A/C E/C		Effect Size	
PD	66,8	30,0	58,5	27,1	47,1	26,7	1	,065	,574	
P-CDI	82,5	21,4	60,5	29,4	43,5	23,9	,018*	,000**	,090	>1
DC	80,2	25,2	57,7	25,8	41,7	27,1	,028*	,000**	,150	>1
PSI TS	79,4	27,1	59,5	25,7	42,4	26,2	,064	,000**	,115	>1

[PD = Parent Distress; P-CDI = Parent-Child Dysfunctional Interaction; DC = Difficult Child; PSI TS = Parental stress index total score]. *p < 0.05 ** p < 0.01

In order to examine the sources of parental stress, we analysed the statistical relationship between PSI scores and other variables. Specifically, we described the correlations between PSI scores and children's age (as continuous variables), drug treatment (as dichotomous variable describing if the child was or was not on drug treatment), the Conners' rating scale scores (as continuous variables describing symptoms) and the MSCS scores (as continuous variables describing self-esteem level). Only some demographic and behavioural variables seem related to parental stress: Table **5** shows the significant correlations. No significant correlations emerged between MSCS and PSI scores.



Scatter Diagram of MSCS subscales in ADHD group.

Table 5. PSI domains and several variable correlation. The table shows only the significant correlations (p< 0,01).

	Children Age	Drug	Conners Opp.
PSI TS	.516		.614
DC (PSI)	.727		.498
P-CDI		.514	.516

[PSI TS = Parental stress index total score; DC= Difficult Child; P-CDI= Parent-Child Dysfunctional Interaction]

Conversely, it appears that higher scores in CPRS oppositional subscale are closely related to higher scores in parental stress level, as measured by "*PSI total score*", "*Difficult Child*" and "*Parent-child dysfunctional interaction*" scores. Furthermore, higher age of children appears related to "*PSI total score*" and "*Difficult Child*" sub-scale scores.

Instead, there were no significant correlations between MSCS scores and other CPRS behavioural sub-domains scores (inattention and hyperactive/impulsive). Finally, the parents of treated children with ADHD show higher stress levels than parents of non-treated children with ADHD, as expressed by the significant correlation between "parentchild dysfunction interaction" and the dichotomous variable describing whether the child was or was not on drug treatment.

DISCUSSION

In accordance with literature supporting the relationship between clinically-diagnosed children with ADHD and low levels of self-esteem, the first purpose of this study was to compare the levels of self-esteem in children with ADHD compared to typically developing and epileptic children. Results suggest that children with ADHD actually have a different level of self-esteem compared to children without ADHD. Self-esteem is both a cognitive and emotional concept that describes the individual's idea and values about him/herself. Self-esteem is also related to cognitive strategies that lead to successful problem-solving, which is a crucial issue in children with ADHD [28]. It is correct to regard selfesteem as a multidimensional concept and to describe different domains of the self-image in different contexts. Low scores in internal domains of self-esteem, such as "psychological well-being" and "skills and talents", have been previously reported in subjects with ADHD [7]. Our results are consistent with the conclusions of a recent paper [31] that describes a significant difference between boys with ADHD and typically developing children on some domains of selfesteem. By the Harter Self-Esteem Questionnaire, reduced scores were found in "Global Self-Esteem Subscale", "Social Acceptance Subscale" and "Scholastic Performance Subscale".

Thus, on an individual level, children with problems related to ADHD seem to have very different profiles of selfesteem, in line with the idea that self-esteem is a multidimensional concept [32]. In this respect, some authors suggest that there is no clear link between ADHD and profiles of self-esteem [7]. They argue that the individual patient with ADHD could have low self-esteem in some domains of selfesteem, but on the whole self-esteem could be quite good. Also in our study, the mean overall MSCS scores of children with ADHD is not greatly impaired, but some subjects out of the whole group showed very low scores. In more details, children with ADHD exhibited lower self-esteem scores in three domains ("Social", "Competence" and "Academic") rather than a global decrease in all areas.

These findings suggest that children's concerns can be focused on developing friendships and good family interactions and school achievements as well. This can be considered a likely consequence of the social and academic failures

A Comparison between Children with ADHD

that children with ADHD commonly have. It is usual for children with ADHD to be criticized and reproached due to their maladaptive behaviours. This condition can lead to develop the idea that nobody appreciates and regards them. Given that children with ADHD lack expertise in most domains, their overly positive self-views of competence promote learning or persistence on difficult tasks that might otherwise prove too discouraging [33].

The only domain in which children with ADHD exhibited a higher self-esteem level than the other two groups was the physical subscale that describes the children's perception of their body and their ability in physical activities. This is a somewhat expected finding since children with ADHD can show good self-confidence in their physical ability due to their high levels of energy and strength. The relatively good self-esteem in physical competence in children with ADHD is in some way consistent with the "positive illusory bias", that is to say that the children have a tendency to overestimate their abilities [12]. In this model it has been argued that the self-enhancement could be a way of neglecting the individual's lack of skills that he/she does not want others to know about [34]. Actually it seems likely that children with ADHD have a really strong perception of their physical power due to their dynamic behavioural pattern and to their get-up-and-go when dealing with peers or older persons.

By examining the mean MSCS score differences between children with ADHD and similar-aged epileptic children, we were able to compare the self-esteem pattern in both social and behavioural domains. As previous studies have reported [19], our results confirm that children with epilepsy do not have a significantly lower self-esteem than the control group even though they have a relatively compromised well-being and comprehensive care needs which go beyond the attempt of controlling seizures. Epilepsy can significantly affect quality of life [21, 35] not only because of its chronicity, the necessity for medication, and their side effects [36], but also due to the prejudices and social conventions that still surround the condition [37].

It is noteworthy that our children with ADHD seem less capable than children with epilepsy to protect themselves from the emotional negative impact of their symptoms on the self-esteem level. Conversely, children with epilepsy showed an even better self-esteem than the typically developing controls in subscale "family" of MSCS. We can assume that the parents of children with epilepsy are more prone to develop reciprocity in the parent-child relationship than the parents of children with ADHD. In fact, they have no reason to feel frustrated and angry because of their "sick" children. Instead, the functional and behavioural problems encountered by children with ADHD can be very disruptive for their families and often lead to conflictive parent-child relationships which can in turn impact children's self-esteem. In fact, when a child displays hyperactivity, inattention, and/or oppositional behaviour, even parents with a high level of care, may respond with dissatisfaction, anger and intolerance. This can lead to a high degree of frustration in children. It is therefore not surprising that the presence of ADHD in children is associated with reduced parenting self-efficacy, lower parental satisfaction and increased levels of parental stress, as indicated by several studies [24, 25]. These suggestions, taken as a whole, propose a possible protective effect on self-esteem as a result of a positive, caring and not frustrated parentchild relationship.

Our study also confirms the relationship between high levels of parental stress and ADHD [38] but does not sustain the relationship between parental stress and child selfesteem. The lack of significant correlations between MSCS and PSI scores suggests that children's self-esteem is not directly influenced by parental stress. This counterintuitive finding could be explained considering that the children's self-esteem level is mostly based on social and academic reinforcements, not only on the well-being of family environment. We could argue that the parental stress have a more modest impact on children's self-idea than the social stigma and the scholastic failure. Given that children build their self-esteem during childhood, and especially during preadolescent and adolescent stage, it is arguable that the behavioral problems could lead to poor peer relations, aggression, and learning problems which are in turn associated with academic failure and a low self-esteem. Previous reports underline how this vicious circle can even have effects on increasing of developing psychiatric disorders, such as depression [39].

Nevertheless, it seems particularly important to understand which variables are more closely related to parental stress. Interestingly in our study, parents of children with ADHD showed higher scores in PSI than parents of children with epilepsy. As correlation analysis reveals, the parental stress levels are mainly associated with oppositional symptoms rather than to inattentive and hyperactive/impulsive behaviours. Children with oppositional defiant disorder (ODD) have frequent run-ins with authority figures and oppositional behaviours, far more often than other children their age. When associated with ODD, ADHD may predispose affected children to the subsequent development of conduct disorders (CDs), delinquent behaviour, and substance misuse [5, 40, 41]. Moreover, children with ODD experience disturbances in peer and family relationships, as well as poor academic achievement [42, 43]. According to other reports, the role of ODD symptoms must be considered of greatest interest is the comorbidity with depression [44] and self-concept weakening [45].

Another interesting figure is that parents stress level increases with the children's age. This finding can be explained considering that adolescents with ADHD usually experience an increasing gap between their functional level and social and academic requirements. The difficulty to cope with this increased demand could consecutively increase parental discomfort and worsen the family relationships.

Finally, an unexpected result showed a higher parental stress level associated with drug treatment. We argue that most parents in Italy still have concerns regarding the safety of medication for treating ADHD and, more in general, a current adverse view of stimulants. Therefore, Italian parents experience stress due to the choice of medication option, even when the treatment shows efficacy in improving symptoms. This evidence is in contrast with a previous North American study [46] that revealed no differences among children on medication and children without medication on measures of family distress (eg, parenting stress, depressive symptoms among parents, marital adjustment).
CONCLUSION

Children with ADHD may be relatively more impaired in self-esteem than other children affected with severe chronic diseases. They can have low self-esteem in some domains of self-esteem, even when the whole self-esteem is not impaired. Thus, the evaluation of self-esteem level in children and adolescents with ADHD can be helpful in guiding psycho-educational interventions that should be individualized and based on a "person-oriented approach" [7]. Timely and targeted treatment for ADHD is associated with improvement of self-esteem and consequently better outcomes [47].

At the same time, it is important to develop intervention programs designed to help parents in the identification and management of their own parenting stress. This seems mostly related to ODD symptoms that cause disturbances in peer and family relationships.

These findings emphasize the psychological aspects of ADHD condition, both in children and in parents and strongly suggest an additional focus on self-esteem problems and on parental stress in the context of a multimodal treatments for children with ADHD.

LIMITATIONS AND IMPLICATIONS FOR RE-SEARCH

The current study is limited by cross-sectional data and by a rather restricted sample. Moreover, our findings in a health care-based sample could describe the characteristics of a more severe form of ADHD with a strong prevalence of combined subtype and of male patients. This is most likely due to the reliance on parents for diagnosis, as teachers identify more problem behaviours in boys, which may contribute to higher numbers of boys treated in clinical settings [48]. Furthermore this paper includes a clinically referred males sample because they are more numerous due to their greater likelihood of disruptive behaviours. Thus, we decided to include only male subjects because females had more internalizing problems, depression, and anxiety as well as diminished self-efficacy and coping, and had less aggression and externalizing behaviors than males [49]. There are few studies addressing the issue of sex differences in self-esteem in children with ADHD. Gershon's (2002) [50] meta-analytic review of gender differences in ADHD revealed females to be rated significantly less impaired than males on hyperactivity, inattention, and impulsivity. This meta analysis found that females with ADHD manifested fewer externalizing problems, and were found to have more internalizing problems. Thus, the relationships among gender, behavior problems, and self-esteem are not well understood and require further research.

CONFLICT OF INTEREST

The authors confirm that this article content has no conflict of interest.

ACKNOWLEDGEMENTS

Declared none.

REFERENCES

- [1] Hoza B. Peer functioning in children with ADHD. J Pediatr Psychol 2007; 32(6): 655-63.
- [2] Shaw-Zirt B, Popali-Lehane L, Chaplin W, Bergman A. Adjustment, social skills, and self-esteem in college students with symptoms of ADHD. J Atten Disord 2005; 8(3): 109-20.
- [3] Galera C, Melchior M, Chastang JF, Bouvard MP, Fombonne E. Childhood and adolescent hyperactivity-inattention symptoms and academic achievement 8 years later: the GAZEL Youth study. Psychol Med 2009; 39(11): 1895-906.
- Barkley RA, Fischer M, Smallish L, Fletcher K. Young adult fol-[4] low-up of hyperactive children: antisocial activities and drug use. J Child Psychol Psychiatry 2004; 45(2): 195-211.
- [5] Barkley RA, Fischer M, Smallish L, Fletcher K. Young adult outcome of hyperactive children: adaptive functioning in major life activities. J Am Acad Child Adolesc Psychiatry 2006; 45(2): 192-202
- [6] Biederman J, Monuteaux MC, Mick E, et al. Young adult outcome of attention deficit hyperactivity disorder: a controlled 10-year follow-up study. Psychol Med 2006; 36(2): 167-79.
- [7] Edbom T, Granlund M, Lichtenstein P, Larsson J-O. ADHD Symptoms Related to Profiles of Self-Esteem in a LOngitudinal Study of Twins, A person-oriented approach. J Child Adolesc Psychiatr Nurs 2008: 228-37.
- [8] Pisecco S, Wristers K, Swank P, Silva PA, Baker DB. The effect of academic self-concept on ADHD and antisocial behaviors in early. J Learn Disabil 2001; 34(5): 450-61.
- Mazzone L, Postorino V, Reale L, et al. Self-esteem evaluation in [9] children and adolescents suffering from ADHD. Clin Pract Epidemiol Ment Health 2013; 9: 96-102.
- [10] Treuting JJ, Hinshaw SP. Depression and self-esteem in boys with attention-deficit/hyperactivity disorder. J Abnorm Child Psychol $2001 \cdot 29(1) \cdot 23-39$
- [11] Hoza B, Pelham WE, Jr., Dobbs J, Owens JS, Pillow DR. Do boys with attention-deficit/hyperactivity disorder have positive illusory. J Abnorm Psychol 2002;111(2): 268-78.
- Hoza B, Vaughn A, Waschbusch DA, Murray-Close D, McCabe G. [12] Can children with ADHD be motivated to reduce bias in selfreports of competence? J Consult Clin Psychol 2012; 80(2): 245-54
- [13] Hoza B, Murray-Close D, Arnold LE, Hinshaw SP, Hechtman L, Group MC. Time-dependent changes in positively biased selfperceptions of children with attention-deficit/hyperactivity disorder: a developmental psychopathology perspective. Dev Psychopathol 2010; 22(2): 375-90.
- [14] Owens JS, Goldfine ME, Evangelista NM, Hoza B, Kaiser NM. A critical review of self-perceptions and the positive illusory bias in children with ADHD. Clin Child Fam Psychol Rev 2007; 10(4): 335-51
- Wolraich ML, Wibbelsman CJ, Brown TE, et al. Attention-[15] deficit/hyperactivity disorder among adolescents: a review of the diagnosis, treatment, and clinical implications. Pediatrics 2005;115(6): 1734-46.
- [16] Houck G, Kendall J, Miller A, Morrell P, Wiebe G. Self-concept in children and adolescents with attention deficit hyperactivity. J Pediatr Nurs 2011; 26(3): 239-47.
- [17] Krueger M, Kendall J. Descriptions of Self: An Exploraty Study of Adolescents with ADHD. JCAI 2001.
- [18] Edbom T, Lichtenstein P, Granlund M, Larsson JO. Long-term relationships between symptoms of Attention Deficit Hyperactivity. Acta Paediatr 2006; 95(6): 650-7.
- [19] Siqueira NF. Guerreiro MM. de Souza EA. Self-esteem, social support perception and seizure controllability perception in. Arq Neuropsiquiatr 2011; 69(5): 770-4.
- Ferro MA, Ferro AL, Boyle MH. A systematic review of self-[20] concept in adolescents with epilepsy. J Pediatr Psychol 2012; 37(9): 945-58.
- [21] Jonsson P, Jonsson B, Eeg-Olofsson O. Psychological and social outcome of epilepsy in well-functioning children and adolescents. A 10-year follow-up study. Eur J Paediatr Neurol 2014; 18(3): 381-90.
- [22] Grue L, Heiberg A. Do disabled adolescents view themsleves differently from other young people? Scand J Disabil Res 2000; 39-57

Clinical Practice & Epidemiology in Mental Health, 2014, Volume 10 183

- [23] Guo W, Wu J, Wang W, et al. The stigma of people with epilepsy is demonstrated at the internalized. Epilepsy Behav 2012; 25(2): 282-8.
- [24] Pimentel MJ, Vieira-Santos S, Santos V, Vale MC. Mothers of children with attention deficit/hyperactivity disorder: relationship. Atten Defic Hyperact Disord 2011; 3(1): 61-8.
- [25] Graziano PA, McNamara JP, Geffken GR, Reid A. Severity of children's ADHD symptoms and parenting stress: a multiple mediation. J Abnorm Child Psychol 2011; 39(7): 1073-83.
- [26] Whalen CK, Odgers CL, Reed PL, Henker B. Dissecting daily distress in mothers of children with ADHD: an electronic diary. J Fam Psychol 2011; 25(3): 402-11.
- [27] Bracken B. Test di Valutazione dell'Autostima. Trento: Edizioni Erickson 1993.
- [28] Bergman LR, Magnusson D, El-Khouri B. Studying individual development in an interindividual context: A person oriented approach. Mahwah, NJ: Erlbaum Associates 2003.
- [29] Abidin R. Parent Stress Index. 3rd ed. Odessa, FL: Psychological Assessment Resources 1995.
- [30] Conners CK. Conners' Rating Scales Revised Techinical Manual. New York: Multi-Health Systems 1997.
- [31] Błachno M, Kołakowski A, Wójtowicz S, et al. [Self-esteem of boys with attention deficit hyperactivity disorder - pilot study]. Psychiatr Pol 2013; 47(2): 281-91.
- [32] Harter S. Cause and consequences of low self-esteem. In: Baumeister R. Ed. Children and adolescents self-esteem: The puzzle of low selfregard. New York: Plenum 1993; pp. 87-116.
- [33] Bjorklund DF. The role of immaturity in human development. Psychol Bull 1997; 122(2): 153-69.
- [34] Asendorpf JB, Ostendorf F. Is self-enhancement healthy? Conceptual, psychometric, and empirical analysis. J Pers Soc Psychol 1998; 74(4): 955-66.
- [35] Taylor J, Jacoby A, Baker GA, Marson AG. Self-reported and parent-reported quality of life of children and adolescents. Epilepsia 2011; 52(8): 1489-98.
- [36] Modi AC, Ingerski LM, Rausch JR, Glauser TA. Treatment factors affecting longitudinal quality of life in new onset pediatric. J Pediatr Psychol 2011; 36(4): 466-75.
- [37] Nurmi J-E, Salmela-Aro K, Haavisto T. The strategy and attribution questionnaire: Psychometric properties. Eur J Psychol Assess 1994: p. 108-21.

Revised: August 08, 2014

Accepted: November 09, 2014

© Gagliano et al.; Licensee Bentham Open.

This is an open access article licensed under the terms of the Creative Commons Attribution Non-Commercial License (http://creativecommons.org/licenses/by-nc/3.0/) which permits unrestricted, non-commercial use, distribution and reproduction in any medium, provided the work is properly cited.

- [38] Deault LC. A systematic review of parenting in relation to the development of comorbidities. Child Psychiatry Hum Dev 2010; 41(2): 168-92.
- [39] LeBlanc N, Morin D. Depressive Symptoms and Associated Factors in Children with Attention Deficit Hyperactivity Disorder. J Child Adolesc Psychiatr Nurs 2004; 49-55.
- [40] Glass K, Flory K, Martin A, Hankin BL. ADHD and comorbid conduct problems among adolescents: associations with. Atten Defic Hyperact Disord 2011; 3(1): 29-39.
- [41] van Lier PA, van der Ende J, Koot HM, Verhulst FC. Which better predicts conduct problems? The relationship of trajectories of. J Child Psychol Psychiatry 2007; 48(6): 601-8.
- [42] Rey J, Walter G, Soutullo C. Oppositional defiant disorder and conduct disorder. Martin A, Volkmar FR, Ed. Lewis's child and adolescent psychiatry. Philadelphia: Lippincott Williams & Wilkins 2007; pp. 454-66.
- [43] van der Oord S, Prins PJ, Oosterlaan J, Emmelkamp PM. The association between parenting stress, depressed mood and informant agreement. Behav Res Ther 2006; 44(11): 1585-95.
- [44] Boylan K, Vaillancourt T, Boyle M, Szatmari P. Comorbidity of internalizing disorders in children with oppositional defiant disorder. Eur Child Adolesc Psychiatry 2007; 16(8): 484-94.
- [45] Chen L, Luo X, Wei Z, et al. Correlation study on behavioral problems and self-concept of children with. Zhong Nan Da Xue Xue Bao Yi Xue Ban 2011; 36(3): 217-22.
- [46] Wells KC, Epstein JN, Hinshaw SP, et al. Parenting and family stress treatment outcomes in attention deficit hyperactivity. J Abnorm Child Psychol 2000; 28(6): 543-53.
- [47] Harpin V, Mazzone L, Raynaud JP, Kahle J, Hodgkins P. Long-Term Outcomes of ADHD: A Systematic Review of Self-Esteem and Social Function. J Atten Disord 2013.
- [48] Derks EM, Hudziak JJ, Boomsma DI. Why more boys than girls with ADHD receive treatment: a study of Dutch twins. Twin Res Hum Genet 2007; 10(5): 765-70.
- [49] Rucklidge JJ. Gender differences in ADHD: implications for psychosocial treatments. Expert Rev Neurother 2008; 8(4): 643-55.
- [50] Gershon J. A meta-analytic review of gender differences in ADHD. J Atten Disord 2002; 5(3): 143-54.

Received: June 30, 2014

Vocal Fold Nodules in School Age Children: Attention Deficit Hyperactivity Disorder as a Potential Risk Factor

Lucia D'Alatri, Livia Petrelli, Lea Calò, Pasqualina Maria Picciotti, Maria Raffaella Marchese, and Francesco Bussu, *Rome, Italy*

Summary: Objective. To evaluate the presence of symptoms of inattention and hyperactivity/impulsivity in a population of school age children affected by vocal fold nodules.

Methods. Parents and teachers of 18 children with vocal fold nodules (10 males, eight females; aged between 6 and 12 years) and 20 matched controls without dysphonia and/or vocal fold diseases (11 males, nine females; aged between 6 and 12 years) completed Attention-Deficit/Hyperactivity Disorder (ADHD) rating scale for parents (SDAG [Scala per i Disturbi di Attenzione/Iperattività per Genitori]) and teachers (SDAI [Scala per i Disturbi di Attenzione/Iperattività per Insegnanti) rating scales containing in two subscales items that specifically evaluate the symptoms of ADHD according to the DSM-IV. All children were subjected to videolaryngoscopy.

Results. The group with vocal fold nodules scored significantly higher than the controls; the difference between the two groups was statistically significant for both the subscales of both questionnaires (SDAG and SDAI) (P < 0.05). Four children in the group with vocal fold nodules who scored higher than 14 in at least one subscale were referred for psychiatric evaluation. For two of the children, both male, a diagnosis of combined ADHD was formulated.

Conclusions. ADHD is a possible risk factor for the development of vocal fold nodules in childhood. SDAG and SDAI rating scales may supplement the diagnostic assessment of children with vocal fold nodules.

Key Words: Vocal fold nodules-Childhood dysphonia-Attention deficit hyperactivity disorder-ADHD.

INTRODUCTION

Studies on the epidemiology of dysphonia in school age children describe a prevalence that ranges widely from six to 38%,^{1–4} reflecting differences in survey methods and in the criteria used for voice evaluation. Most authors, however, estimate a prevalence of 6-9%.⁴

Vocal fold nodules represent the most common laryngeal cause of voice disorders in children^{4,5}; between 38% and 78% of children evaluated for chronic hoarseness are estimated to have vocal fold nodules.⁶ Nodules are characterized by bilateral thickening at the junction of the anterior and middle thirds of the vocal folds. Histological analyses of vocal fold nodules have revealed proliferation of the epithelial layers, thickening of the basal membrane and the presence of fibronectin in the superficial layer of the lamina propria.⁷

Vocal fold nodules are associated with chronic vocal abuse or misuse.^{8,9} Vocal abuse can be described as yelling, talking in excess, singing, laughing, crying, cheering, imitating animal noises, and making sound effects. The quality of communicative interactions in the family, the child's personality, and the way he/she asserts him/herself may be other determinants of hyperfunctional vocal behavior. Moreover, effort and mechanical traumatism in phonation may be exacerbated by different factors such as recurrent infections of the upper airways, allergies, gastroesophageal reflux, hearing

Journal of Voice, Vol. 29, No. 3, pp. 287-291 0892-1997/\$36.00

© 2015 The Voice Foundation

http://dx.doi.org/10.1016/j.jvoice.2014.07.019

impairment, velopharyngeal insufficiency, and pollution from environmental noise. In addition, the characteristics of a child's larynx (ie, immaturity of intrinsic muscles and incomplete development of the vocal ligament) make it more vulnerable to phonotrauma.¹⁰

Literature data about pediatric hyperfunctional dysphonia indicate a predominance of males (57–64%) over females (36–43%) with a ratio close to $2:1.^{8,9,11}$ These findings could be related to the impulsive and aggressive behavior often associated with hyperactivity, anxiety, and spirit of leadership among boys.¹²

Voice therapy is part of the recommended therapeutic strategy for vocal fold nodules in children.^{13–15} Vocal hygiene, including the avoidance of voice abuse, is another relevant component of treatment. Involvement of parents and teachers is important in treatment planning. However, the psychological traits of dysphonic children are likely to make them noncompliant to active voice therapy and vocal hygiene recommendations.^{16,17}

Attention deficit hyperactivity disorder (ADHD) is one of the most common psychiatric disorders in children and adolescents.^{18–20} A recent systematic review showed that in 2010, the ADHD worldwide pooled prevalence for the age range 5–19 years was 2.2% (2.0–2.3) and 0.7% (0.6–0.7) for males and females, respectively.²¹ ADHD is characterized by either significant inattention, hyperactivity, impulsiveness, or a combination of these traits.^{18–20,22} According to the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV-TR),²² ADHD symptoms emerge before 7 years of age, must manifest in at least two separate settings and must result in an impairment in one or more functional domains. Inattention is characterized by difficulties in remaining focused, poor attention to detail, inability to work on the same task for an extended period

Accepted for publication July 30, 2014.

From the ENT and Ophthalmology Department, Institute of Otorhinolaryngology, Policlinico "A. Gemelli", Catholic University of Sacred Heart, Rome, Italy.

Address correspondence and reprint requests to Livia Petrelli, Policlinico "A. Gemelli", Università Cattolica del Sacro Cuore, Largo Gemelli n.8, Rome 00168, Italy. E-mail: livia83@hotmail.it

of time, difficulty in performing actions, rapid onset of fatigue, and boredom.^{18–20,22} Hyperactivity is characterized by constant and excessive motor activity and the inability to respect the rules, time, and space of others.^{18–20,22} Impulsivity, often linked to hyperactivity, manifests as a difficulty in avoiding dangerous situations, a tendency to move quickly from one activity to another and a tendency to talk too much with poor control of vocal intensity.^{18–20,22}

Although the finding that children with vocal fold nodules are impulsive and aggressive is quite common among clinicians,^{9,23,24} there are few objective data to reject or promote the hypothesis that a behavioral disorder may underlie the development of vocal fold nodules in children. Although the association between vocal fold nodules and personality traits, such as elevated social dominance, emotional reactivity, aggressiveness and impulsivity, has been described in women,^{25,26} the relationship between specific personality traits and the development of vocal fold nodules still needs to be confirmed in children.²⁷

In this study, using parents' and teachers' rating scales, we investigated the presence of symptoms of inattention and hyperactivity/impulsivity in a population of school age children affected by vocal fold nodules and in a vocally healthy control group.

METHODS

The research described in the following was reviewed and approved by the Local Review Board at the Catholic University of the Sacred Heart and was conducted according to the principles expressed in the Declaration of Helsinki. Permission was obtained from the school authorities and parents or guardians of the children.

During a period of 6 months, 32 children (18 males, 14 females; mean age 6.72 ± 4.22 years) affected by dysphonia were referred to our speech and language disorders unit. All patients underwent the following:

- Collection of clinical history, to specifically analyze speech and language development, and the behavioral characteristics and vocal attitudes of the child and his/ her family;
- ENT examination of the upper airways including flexible fiberoptic videolaryngoscopy without stroboscopy (model RLS 9100B; Kay Elemetrics Corp., Lincoln Park, NJ);
- A perceptual evaluation, performed on recorded voice samples by a panel of three speech therapists with a minimum of 3 years of clinical experience in children's voice therapy, using the GRBAS (Grade, Roughness, Breathiness, Asthenicity, Strain) scale²⁸;
- Audiological evaluation.

Eighteen of the 32 children (10 males, eight females) were included in the study and were designated as group A. The inclusion criteria for the recruitment of children into group A were as follows: age between 6 and 12 years; bilateral vocal fold nodules; history of dysphonia for at least 12 months; no previous voice therapy; normal hearing, as measured through behavioral sound field audiometry and defined as an auditory threshold ≤ 20 dB nHL at all tested frequencies (250–4000 Hz); no history of recurrent inflammation of the upper airway, allergies, and gastroesophageal reflux; and the absence of bronchopulmonary diseases.

The control group, group B, was composed of 20 children (11 males, nine females) randomly selected from all of the children who periodically came to the hospital's pediatrics department for wellness visits. The inclusion criteria of these children were the same as for children in group A without, of course, any report of dysphonia or vocal fold nodules. Moreover, before inclusion as a control subject, the child's voice had to be judged as normal by three speech therapists. Specifically, the control subjects had to be classified by a 0 score in all of the GRBAS items by all of the speech therapists.

After obtaining informed consent from the parents, two screening questionnaires addressing DSM IV criteria for ADHD, SDAG (Scala per i Disturbi di Attenzione/ Iperattività per Genitori [ADHD rating scale for Parents]) and SDAI (Scala per i Disturbi di Attenzione/Iperattività per Insegnanti [ADHD rating scale for Teachers])²⁹ (Figure 1), were completed by the parents and teachers of the children in both groups. The two scales, validated and standardized for the Italian population, are similar in organization and scope to those widely used in other countries.³⁰ Both tools contained 18 items that closely mirror the DSM-IV ADHD symptoms.³¹ In each scale, nine items (marked with odd numbers) explore Inattention (subscale In), and nine items (marked with even numbers) explore Hyperactivity/Impulsivity (subscale H/I). Frequency and intensity of the 18 ADHD symptoms are rated on a 4-point Likert scale from 0 to 3 (0, never, 1, sometimes, 2, often, 3, very often). Therefore the overall scores for subscale In and subscale H/I of the SDAG and SDAI rating scales may vary from 0 to 27. The cut-off for considering a child for a possible diagnosis of ADHD and for referring him/ her to a psychiatrist is represented by a score above 14 in at least one subscale. In the patient group, we looked for correlations between GRBAS scores and scores from the four subscales.

Statistical analysis

For comparisons between groups, the Student *t* test for unpaired samples was used. Correlation between numerical variables (GRBAS and SDAI/SDAG scores) was evaluated by linear bivariate fit and analysis of variance. The level of significance was set at P < 0.05. The statistical package *MedCalc* (MedCalc Software bvba, Marienkerke, Belgium) was used.

RESULTS

The two groups did not differ significantly in age (mean age of group A = 8.83 ± 2.15 years; mean age of group B = 8.45 ± 1.57 years; P > 0.05) or gender (P > 0.05).

The comparison between groups showed that the mean scores of group A were higher for subscales In and H/I of the

nti) (ADHD rating scale for Teac

SDAG (Scala per i Disturbi di Attenzione/Iperattività per Genitori) (ADHD rating scale for Parents)

	son (search per rolstand an Attention of Perattinia per insegnanti) (non brank search of reacters)
 Incontra difficoltà nell'esecuzione di attività che richiedono una certa cura. 	1. Incontra difficoltà a concentrare l'attenzione sui dettagli o compie errori di negligenza.
He/she faces considerable difficulty in performing activities requiring attention.	He/she fails to give close attention to details or makes careless mistakes in schoolwork.
2. Spesso a tavola o alla scrivania, durante lo svolgimento dei compiti, si agita con le mani (ad esempio,	2. Spesso si agita con le mani o i piedi o si dimena sulla sedia.
giocherellando con gli oggetti che gli sono vicini afferrando le cose in modo maldestro), o con i piedi, o si dimena sulla	He/she fidgets with hands or feet or squirms in the seat.
sedia.	 Incontra difficoltà nel mantenere l'attenzione sui compiti o sui giochi in cui è impegnato.
While performing the homework at the desk, he/she fidgets with hands (i.e. fiddling with close objects or grasping	He/she faces considerable difficulty sustaining attention in tasks or play activities.
things) or feet or squirms in the seat.	4. Non riesce a stare seduto.
3. Incontra difficoltà nel mantenere l'attenzione sui compiti o sui giochi in cui è impegnato, interrompendosi	He/she leaves seat in classroom.
ripetutamente o passando di frequente ad attività differenti.	5. Quando gli si parla non sembra ascoltare.
He/she faces considerable difficulty in staying tuned on tasks or games, repeatedly breaking off and/or changing	He/she does not seem to listen when spoken to directly.
activity.	6. Manifesta una irrequietudine interna, correndo o arrampicandosi dappertutto.
 Non riesce a stare seduto quando le circostanze lo richiedono. 	He/she looks restless. runnina and climbina all around.
He/she cannot keep his/her seat when required by circumstances.	7. Pur avendo capito le istruzioni e non avendo intenzioni oppositive, non segue le istruzioni ricevute o fatica a
5. Quando gli si parla non sembra ascoltare.	portarle a compimento.
He/she does not seem to listen when somebody speaks to him directly.	He/she does not follow through on instructions or can barely accomplish them (not due to oppositional behaviour
6. Manifesta una irrequietudine interna, correndo o arrampicandosi dappertutto.	or failure of comprehension).
He/she looks restless, running and climbing all around.	 Incontra difficoltà a impegnarsi in attività o in giochi tranquilli.
7. Non esegue ciò che gli viene richiesto o fatica a portarlo a compimento.	He/she faces considerable difficulty playing or engaging in quiet leisure activities.
He/she cannot accomplish at all or barely accomplishes what is required.	9. Incontra difficoltà a organizzarsi nei compiti e nelle sue attività.
8. Incontra difficoltà a impegnarsi in attività o in giochi tranquilli.	He/she faces considerable difficulty in scheduling tasks and activities.
He/she faces considerable difficulty playing or engaging in quiet leisure activities.	10. È in movimento continuo come se avesse dentro un motorino che non si ferma.
9. Incontra difficoltà a organizzarsi nei compiti e nelle sue attività.	He/she is "on the go" or acts as if "driven by a motor."
He/she faces considerable difficulty in scheduling tasks and activities.	11. Evita o è poco disposto a impegnarsi in attività che richiedono uno sforzo continuato.
10. Si muove continuamente come se avesse l' "argento vivo" addosso.	He/she avoids or is reluctant to engage in tasks that require sustained mental effort.
He/she is "on the go" or has the fidgets .	12. Parla eccessivamente.
11. Evita o è poco disposto a impegnarsi in attività che richiedono uno sforzo continuato.	He/she talks excessively.
He/she avoids or does not engage him/herself in tasks that require sustained mental effort.	13. Perde oggetti necessari per le attività che deve svolgere.
12. Non riesce a stare in silenzio; parla eccessivamente.	He/she loses things necessary for tasks or activities.
He/she cannot remain quiet and talks excessively.	14. Risponde precipitosamente prima ancora che la domanda sia stata interamente formulata.
13. Non tiene in ordine le sue cose e di conseguenza le perde.	He/she blurts out answers before questions have been completed.
He/she does not keep things tidy and therefore loses them.	15. Viene distratto facilmente da stimoli esterni.
14. Risponde precipitosamente.	He/she is easily distracted by extraneous stimuli.
He/she blurts out answers.	16. Non riesce a rispettare il proprio turno.
15. Viene distratto facilmente da stimoli esterni.	He/she has difficulty awaiting turn.
He/she is easily distracted by extraneous stimuli.	17. Tende a dimenticarsi di fare le cose.
16. Non riesce a rispettare il proprio turno.	He/she is forgetful in daily activities.
He/she has difficulty awaiting turn.	18. Spesso interrompe o si comporta in modo invadente con altre persone impegnate in un gioco o in una
17. Trascura o dimentica le incombenze o i compiti di ogni giorno.	conversazione.
He/she is forgetful in daily activities.	He/she interrupts or intrudes on others engaged in a game or in a conversation.
18. Spesso interrompe o si comporta in modo invadente con altre persone (fratelli, genitori, amici) impegnate in un	
gioco o in una conversazione.	
He/she interrunts or intrudes on others (brothers, parents, friends) engaged in a game or in a conversation.	

SDAI (Scala per i Disturbi di Attenzione/Inerattività per Insegn

FIGURE 1. SDAG and SDAI questionnaires addressing the DSM IV criteria for attention deficit hyperactivity disorder. In bold an indicative English translation (not validated for clinical use) is shown.

SDAG and SDAI questionnaires. This difference between the two groups was statistically significant for both subscales of both questionnaires (P < 0.05) (Table 1). In Figures 2 and 3, the individual scores obtained from the children of group A and B, respectively, are reported.

Four of the eighteen children (22.22%) of group A scored higher than 14 in one or both subscales of the SDAG and SDAI questionnaires. In particular, two 7 year-old boys (cases 11 and 18; Figure 2) had scores higher than 14 in both subscales of both questionnaires. For one 11 year-old male (case 6; Figure 2), a score higher than 14 was obtained in the subscale H/I of the SDAG questionnaire and in both subscales of the

TABLE 1.

Group A and Group B Mean Scores and Standard
Deviations Obtained in Subscales In and H/I of SDAG and
SDAI Questionnaires

Subscale	Group A (n = 18)	$\begin{array}{l} \text{Group B} \\ \text{(n}=\text{20)} \end{array}$	Ρ
SDAG subscale In	8.17 ± 5.11	4.25 ± 2.00	0.003
SDAG subscale H/I	8.33 ± 554	4.10 ± 1.52	0.002
SDAI subscale In	8.56 ± 5.35	3.50 ± 2.09	<0.001
SDAI subscale H/I	8.61 ± 5.35	4.25 ± 2.57	0.002

Abbreviations: SDAG, Scala per i Disturbi di Attenzione/Iperattività per Genitori (ADHD rating scale for parents); SDAI, Scala per i Disturbi di Attenzione/Iperattività per Insegnanti (ADHD rating scale for teachers); In, Inattention; H/I, Hyperactivity/Impulsivity. SDAI questionnaire. Finally, a 10 year-old girl (case 8; Figure 2) had a score greater than 14 in the subscale In of the SDAG questionnaire and in both subscales of the SDAI questionnaire.

These four children in group A who scored higher than 14 in the screening questionnaires were referred to a psychiatrist for further evaluation. For two of the children (cases 11 and 18; Figure 2), both of whom were male, a diagnosis of combined ADHD was made according to the DSM-IV-TR criteria.²²

After evaluating the scores of the SDAI and SDAG subscales and the scores of the GRBAS perceptual evaluation, no statistical significance emerged. Nevertheless, a trend toward a correlation between higher scores in the subscale H/I of the questionnaire for teachers (SDAI) and more relevant alterations in G (P = 0.09), B (P = 0.08), and S (P = 0.09) items was observed.

DISCUSSION

In this study, we investigated the presence of symptoms of inattention, hyperactivity, and impulsivity in a population of school age children affected by vocal fold nodules and in a sex- and age-matched control group. Recruitment of dysphonic children in the study was performed based on vocal symptoms duration (at least 12 months) and after precluding other organic causes of dysphonia (eg, inflammation of upper airway, allergies, gastroesophageal reflux, bronchopulmonary diseases, and/or hearing impairment). We found that children with vocal



FIGURE 2. Group A (n = 18): individual scores obtained in the subscales Inattention (In) and Hyperactivity/Impulsivity (H/I) of SDAG and SDAI questionnaires. SDAG, Scala per i Disturbi di Attenzione/Iperattività per Genitori (ADHD rating scale for parents); SDAI, Scala per i Disturbi di Attenzione/Iperattività per Insegnanti (ADHD rating scale for teachers); In, Inattention; H/I, Hyperactivity/Impulsivity.

fold nodules scored significantly higher in the SDAG and SDAI rating scales than euphonic children. Moreover, 11.11% of children with vocal fold nodules were affected by combined ADHD subtype.

Voice therapy is the treatment of choice for vocal fold nodules.^{13,14} The purpose of voice therapy is to optimize laryngeal function, mainly by reducing hyperfunction, which produces chronic traumatism, so that the size of the nodules will decrease and surgery will be avoided.³² However, vocal fold nodules in children are often resistant to treatment and tend to recur.^{32–34} As behavioral voice therapy requires time, energy, and money, it is important to better understand the factors involved in nodule development and maintenance. Voice therapy failure in children is frequently related to the lack of self-regulatory behavior and impulse control, which does not allow for reducing phonotraumatic behaviors.¹⁷ Accordingly, vocal hygiene counseling plays just as important a role as vocal exercises. Literature data show that children with hyperfunctional dysphonia, with or without vocal fold nodules, more frequently possess characteristics such as talkativeness, hyperactivity, aggressiveness, impulsivity, immaturity in their ability to address everyday stressful situations, and reduced ability for effective emotional control and harmonious interaction with others.^{9,23,24} For this reason, Niedzielski et al³⁵ suggested that psychotherapy may supplement traditional voice therapy in the treatment of vocal fold nodules in children.

The relationship between vocal and behavioral disorders has been recently described by Hamdan et al³⁶ These authors performed a study of 19 children with combined ADHD and 19 age- and gender-matched controls. They found that the voices of children with ADHD were perceived to have a significantly higher degree of hoarseness, breathiness, and straining. Moreover, compared with the healthy group, ADHD children also had louder voices.

Our report represents a preliminary investigation with a limited sample size, and further research with a larger number



FIGURE 3. Group B (n = 20): individual scores obtained in subscales In and H/I of SDAG and SDAI questionnaires. SDAG, Scala per i Disturbi di Attenzione/Iperattività per Genitori (ADHD rating scale for parents); SDAI, Scala per i Disturbi di Attenzione/Iperattività per Insegnanti (ADHD rating scale for teachers); In, Inattention; H/I, Hyperactivity/Impulsivity.

of dysphonic children, with and without vocal fold nodules, is needed to confirm these hypotheses. Nevertheless, the present results are consistent with the findings of Hamdan et al³⁶ and, more recently, of Teresa Garcia-Real et al³⁷ and suggest that ADHD is a potential risk factor for the onset of hyperfunctional dysphonia and vocal fold nodules in children. Some of our results, which deserve to be confirmed through larger studies, suggest that questionnaires administered to teachers may prove to be more valuable in assessing such risk.

Diagnostic assessment of childhood dysphonia usually includes laryngeal examination, using flexible or rigid laryngoscopy, subjective evaluation of voice characteristics, acoustic analysis, and parent rating reports such as Pediatric Voice Handicap Index.³⁸ The data from this preliminary study indicate that it would be worthwhile to include SDAG and SDAI or other analogous rating scales for the diagnosis of ADHD in the clinical evaluation of children with hyperfunctional dysphonia with or without vocal fold nodules. If ADHD is suspected, children should undergo psychiatric assessment to set up a multimodal management plan as voice therapy alone may not be sufficient.

REFERENCES

- Senturia BH, Wilson FB. Otorhinolaryngic findings in children with voice deviations. Preliminary report. Ann Otol Rhinol Laryngol. 1968;77: 1027–1041.
- Nilson H, Schneiderman CR. Classroom program for the prevention of vocal abuse in elementary school children. *Lang Speech Hear Serv Sch.* 1983;14:172–178.
- Carding PN, Roulstone S, Northstone K, ALSPAC study team. The prevalence of childhood dysphonia: a cross-sectional study. J Voice. 2006;20: 623–630.
- Akif Kiliç M, Güzelsoy S. The prevalence of vocal fold nodules in school age children. Int J Pediatr Otorhinolaryngol. 2004;68:409–412.
- Dobres R, Lee L, Stemple JC, Kummer AW, Kretschmer LW. Description of laryngeal pathologies in children evaluated by otolaryngologists. J Speech Hear Disord. 1990;55:526–532.
- 6. Von Leden H. Vocal nodules in children. *Ear Nose Throat J.* 1985;64: 473–480.
- Martins RH, Defaveri J, Custódio Domingues MA, de Albuquerque E Silva R, Fabro A. Vocal fold nodules: morphological and immunohistochemical investigations. *J Voice*. 2010;24:531–539.
- Connelly A, Clemente WA, Kubba H. Management of dysphonia in children. J Laryngol Otol. 2009;123:642–647.
- Angelillo N, Di Costanzo B, Angelillo M, Costa G, Barillari MR, Barillari U. Epidemiological study on vocal disorders in pediatric age. J Prev Med Hyg. 2008;49:1–5.
- Trani M, Ghidini A, Bergamini G, Presutti L. Voice therapy in pediatric functional dysphonia: a prospective study. *Int J Pediatr Otorhinolaryngol*. 2007;7:379–384.
- Ahrens P, Seibt Y, Kitz R. Vocal cord dysfunction in children and adolescents. *Pneumologie*. 2001;55:378–384.
- Martins RH, Hidalgo Ribeiro CB, Fernandes de Mello BM, Branco A, Tavares EL. Dysphonia in children. J Voice. 2012;26:674.e17–674.e20.
- Colton HR, Casper JK, Leonard R. Understanding Voice Problems: A Physiological Perspective for Diagnosis and Treatment. 4th ed. Alphen aan den Rijn: Lippincott Williams & Wilkins; 2011.
- Signorelli ME, Madill CJ, McCabe P. The management of vocal fold nodules in children: a national survey of speech-language pathologists. *Int J* Speech Lang Pathol. 2011;13:227–238.

- Akin Şenkal O, Ciyiltepe M. Effects of voice therapy in school-age children. J Voice. 2013;27:787.e19-25.
- Hirschberg J, Dejonckere PH, Hirano M, Mori K, Schultz-Coulon HJ, Vrticka K. Voice disorders in children. Int J Pediatr Otorhinolaryngol. 1995;32:S109–S125.
- Verdolini K, Li N, Hersan R, Kessler L. Voice therapy for children. In: Hartnick C, Boseley M, eds. *Clinical Management of Children's Voice Disorders*. San Diego, CA: Plural Publishing; 2010.
- Biederman J, Faraone SV. Attention-deficit hyperactivity disorder. *Lancet*. 2005;366:237–248.
- De la Barra FE, Vicente B, Saldivia S, Melipillan R. Epidemiology of ADHD in Chilean children and adolescents. *Atten Defic Hyperact Disord*. 2013;5:1–8.
- Bianchini R, Postorino V, Grasso R, et al. Prevalence of ADHD in a sample of Italian students: a population-based study. *Res Dev Disabil*. 2013;34: 2543–2550.
- Erskine HE, Ferrari AJ, Nelson P, et al. Research Review: Epidemiological modelling of attention-deficit/hyperactivity disorder and conduct disorder for the Global Burden of Disease Study 2010. J Child Psychol Psychiatry. 2013;54:1263–1274.
- American Psychiatric Association. *Diagnostic and Statistical Manual of* Mental Disorders. 4th ed. Washington, DC: American Psychiatric Association Press; 2000.
- Nemec J. The motivation background of hyperkinetic dysphonia in children: a contribution to psychologic research in phoniatry. *Logos.* 1961;4: 28–31.
- 24. Green G. Psycho-behavioral characteristics of children with vocal nodules: WPBIC ratings. J Speech Hear Disord. 1989;54:306–312.
- Roy N, Bless DM, Heisey D. Personality and voice disorders: a superfactor trait analysis. J Speech Lang Hear Res. 2000;43:749–768.
- Roy N, Bless DM, Heisey D. Personality and voice disorders: a multitraitmultidisorder analysis. J Voice. 2000;14:521–548.
- Roy N, Holt KI, Redmond S, Muntz H. Behavioral characteristics of children with vocal fold nodules. J Voice. 2007;21:157–168.
- Hirano M. Psycho-acoustic evaluation of voice: GRBAS scale for evaluating the hoarse voice. In: Hirano M, ed. *Clinical Examination of Voice*. New York, NY: Springer-Verlag; 1981:81–84.
- 29. Marzocchi GM, Cornoldi C. Una scala di facile uso per insegnanti per la segnalazione di bambini con deficit di attenzione/iperattività. [An easy teacher rating scale for the identification of ADHD children]. *Psicologia Clinica dello Sviluppo* [Italian]. 2000;4:43–64.
- DuPaul GJ, Power TJ, Anastopoulos AD. ADHD Rating Scale IV. New York, NY: Guilford Publications; 1998.
- American Psychiatric Association. *Diagnostic and Statistical Manual of* Mental Disorders (DSM-IV). 4th ed. Washington, DC: American Psychiatric Association Press; 1994.
- Ramig LO, Verdolini K. Treatment efficacy: voice disorders. J Speech Lang Hear Res. 1998;41:S101–S116.
- Deal RE, McClain B, Sudderth JF. Identification, evaluation, therapy, and follow-up for children with vocal nodules in a public school setting. J Speech Hear Disord. 1976;41:390–397.
- Wohl DL. Nonsurgical management of pediatric vocal fold nodules. Arch Otolaryngol Head Neck Surg. 2005;131:68–70.
- Niedzielski A, Niedzielska G, Gwizda G. Personality features of children treated due to vocal nodules. Ann Univ Mariae Curie Sklodowska Med. 2002;57:53–57.
- Hamdan AL, Deeb R, Sibai A, Rameh C, Rifai H, Fayyad J. Vocal characteristics in children with attention deficit hyperactivity disorder. *J Voice*. 2009;23:190–194.
- Garcia-Real T, Diaz-Roman TM, Garcia-Martinez V, Vieiro-Iglesias P. Clinical and acoustic vocal profile in children with attention deficit hyperactivity disorder. J Voice. 2013;27:787.e11–787.e18.
- Zur KB, Cotton S, Kelchner L, Baker S, Weinrich B, Lee L. Pediatric voice handicap index (pVHI): a new tool for evaluating pediatric dysphonia. *Int J Pediatr Otorhinolaryngol.* 2007;71:77–82.

Stress levels in parents of children with and without attention-deficit/hyperactivity disorder during the back-to-school period: results of an international survey in Italy

Urania Loprieno^a, Antonella Gagliano^{b*}

^aClinical Development and Medical Affairs, Shire, Florence, Italy, email

ULoprieno@shire.com; ^bUniversity of Messina, Messina, Italy

*Author for correspondence

Professor Antonella Gagliano

Divisione di Psichiatria dell'Infanzia e dell'Adolescenza, Università di Messina

Via Consolare Valeria

98125 Messina

Italy

Tel: +39 328 9474933

Fax: +39 090 2930414

E-mail: agagliano@unime.it

Journal

Minerva Pediatrica

Previous presentations of data

Data were presented at the following congresses:

- 68th National Congress of the Italian Society of Paediatrics (SIP), Rome, Italy, 9–11 May 2012
- 4th ADHD Workshop 'From evidence to clinical practice', Cagliari, Italy, 8–10 March 2012,

Suggested category: Original article

Short title (no length suggested, no abbreviations):

his document is protected by international copyright laws. No additional reproduction is authorized. It is permitted for personal use to download and save only one file and print only or topy of this Article. It is not permitted to make additional copies (either sporadically or systematically, either printed or electronic) of the Article for any purpose. It is not permitted to distribute the electronic copy of the article through online internet and/or intranet file sharing systems, electronic mailing or any other means which may a ow access to the Article. The use of all or ar

Back-to-school stress levels in parents of children with and without attentiondeficit/hyperactivity disorder in Italy

Conflicts of Interest

U Loprieno is an employee of Shire. A Gagliano has received research grants from Shire Development Ltd and has been a speaker for Novartis and Shire Development Ltd.

Funding and Acknowledgements

The research was funded by Shire International GmbH, Switzerland. Ipsos MORI (London, UK) carried out fieldwork and data collection but was not responsible for the analysis or reporting of results. McCann Manchester was employed by Shire to manage the back-to-school stress survey project. Under the direction of the authors, Monica Guidi, PhD, and Alyson Bexfield, PhD, employees of Caudex Medical, Oxford, UK provided writing assistance for this publication. Editorial assistance in formatting, proofreading and copyediting was also provided by Caudex Medical. Shire International GmbH, Switzerland provided funding to Caudex Medical, Oxford, UK for support in writing and editing this manuscript. The content of this manuscript, the ultimate interpretation, and the decision to submit it for publication in *Minerva Pediatrica* was made by the authors independently.

Author information

AG is Assistant Professor of Research in Child and Adolescent Psychiatry in the Department of Pediatric Science, University of Messina, Policlinico Universitario G. Martino UL is a full-time employee of Shire. Shire develops and manufactures treatments for psychiatric disorders including ADHD.

his document is protected by international copyright laws. No additional reproduction is authorized. It is permitted for personal use to download and save only one file and print only or copy of this Article. It is not permitted to make additional copies (either sporadically or systematically, either printed or electronic) of the Article for any purpose. It is not permitted to distributhe electronic copy of the uticle through on ne internet and/or intranet file sharing systems, electronic maining or any other means which may allow access to the Article. The use of all or ar

Authors' contributions

AG had input into the design of the study. Both authors contributed to the analysis and interpretation of data, critically reviewed the manuscript for intellectual content and approved the manuscript for publication.

Word limit: 3000-5500 words, not including references, tables or figures (currently: 3747 words). Maximum 50 references (currently 34)

Summary

Abstract should be 200-250 words (currently 249 words).

Aim: The back-to-school stress survey was an international, non-clinical opinion survey, which aimed to compare stress levels in parents of children with/without attention-deficit/hyperactivity disorder (ADHD) during the back-to-school period. Here, we present results relating to the Italian sample, comparing them with European data.

Methods: The questionnaire was built using a modified Holmes and Rahe stress scale. Parents of children with/without ADHD evaluated potentially stress-causing situations on a scale from 1 (low stress) to 10 (high stress).

Results: In Italy, 107 parents of children with ADHD (mean age [SD]: 40.3 [7.3] years) and 105 parents of children without ADHD (mean age [SD]: 42.2 [6.6] years) participated in the survey. The mean age (SD) of children with ADHD was 10.3 (3.1) years; 77.6% were male, 72.9% had been diagnosed with at least one comorbid condition – in particular conduct disorder (24.3%), learning disorders/dyslexia (23.4%) and language/communication disorder (19.6%) – and 32.7% were receiving ADHD medication. Parents of children with ADHD showed significantly higher stress levels ($p \le 0.005$) compared with the non-ADHD group in all areas analysed that were related to the return to school. Significant differences between

his document is protected by international copyright laws. No additional reproduction is authorized. It is permitted for personal use to download and save only one file and print only or copy of this Article. It is not permitted to make additional copies (either sporadically or systematically, either printed or electronic) of the Article for any purpose. It is not permitted to distributhe electronic copy of the article through on the internet and/or intranet file sharing systems, electronic main give any other means which may allow access to the Article. The use of all or ar groups (p<0.05) were also observed in most standard areas evaluated (e.g. personal life). These results were in agreement with data obtained for the overall European sample. **Conclusions:** Parents of children with ADHD suffer significantly higher stress levels compared with parents of children without ADHD. Considering parental stress is important for the management of children with ADHD, as stress can affect the control of behavioural symptoms of children.

Keywords (MeSH)

Attention deficit hyperactivity disorder; parenting; stress, psychological; questionnaires; schools

his document is protected by international copyright laws. No additional reproduction is authorized. It is permitted for personal use to down oad and save only one file and print only or copy of this Article. It is not permitted to make additional copies (either sporadically or systematically, either printed or electronic) of the Article forony purpose. It is not permitted to distributhe electronic copy of the article through online internet and/or intranet fle sharing systems, electronic mailing or any other means which may allow access to the Article. The use of oll or ar

Introduction

Attention-deficit/hyperactivity disorder (ADHD) is one of the most common neurobehavioural conditions in childhood and adolescence, with an estimated global prevalence of 3–5%.^{1, 2} It is characterized by persistent symptoms of inattention, hyperactivity and impulsivity^{3, 4} that can cause significant impairment in different areas of life. ADHD symptoms are often accompanied by comorbid conditions,⁵ which are associated with substantial functional impairment and complicate the clinical presentation and diagnosis.

The perception of ADHD varies across world regions, with consequent differences in prevalence estimates, diagnostic criteria, clinical guidelines and availability of pharmacological agents.⁶ In Italy, official figures from the Ministry of Health, based on studies conducted between 1993 and 2003, acknowledge a relatively low prevalence of the disorder of 1% of the child and adolescent population (6–18 years old).⁷ Likewise, a more recent study in Northern Italy presented a prevalence estimate of 0.95% in a similar age group (6–17 years old),⁸ while the PrISMA study, which assessed psychiatric disorders in 3418 Italian adolescents, showed a prevalence of 1.2% for externalizing disorders as a whole.⁹ Other works, however, report a higher prevalence of ADHD in Italy; for example, 5.6% of children aged 6–11 years¹⁰ and 3% of children aged 5–15 years.¹¹

In general, both pharmacological (in particular stimulants) and psychological (e.g. parent training, behavioural interventions and cognitive behavioural therapy) therapies are considered effective for the treatment of ADHD, but their relative role in disease management differs between countries. In Europe, pharmacotherapy is considered as first-line treatment only for patients with severe symptoms and impairment, or those who do not respond to non-pharmacological interventions.^{12, 13} In Italy, diagnostic and treatment

his document is protected by international copyright laws. No additional reproduction is authorized. It is permitted for personal use to download and save only one file and print only or topy of this Article. It is not permitted to make additional copies (either sporadically or systematically, either printed or electronic) of the Article for any purpose. It is not permitted to distribut the electronic copy of the article through on the internet and/or intranet file sharing systems, electronic mailing or any other means which may allow access to the Article. The use of all or ar processes are particularly controlled; ADHD diagnoses can be made only at regional referral centres approved by the Ministry of Health, and patients must be enrolled in an ADHD medication registry before pharmacological treatment can be prescribed.¹⁴ The only medications currently approved in Italy for the treatment of ADHD are immediate-release methylphenidate (Ritalin 10 mg capsules, Novartis Farma SpA, Origgio, Italy), extended release methylphenidate (Equasym 10, 20 or 30 mg modified release capsules, Shire Italy SpA, Florence, Italy) and atomoxetine (Strattera 10, 18, 25, 40, 60, 80, or 100 mg capsules, Eli Lilly Italia SpA, Florence, Italy).^{14, 15}

Although ADHD symptoms are visible in pre-school children, they generally become more apparent and problematic when children start going to school, where they typically have more difficulties with successful learning compared with their peers, show aggressive behaviour, and experience peer-rejection and low self-esteem.¹⁶ School problems can have important consequences later in life, with ADHD associated with a greater risk of lower educational achievement and employment status.^{17, 18}

Functional and behavioural problems encountered by children with ADHD can be very disruptive for their families and often lead to conflictive parent–child relationships. Parents may find it difficult to get help from other family members, while children with ADHD tend to have difficulty finding friends due to their poor social and behavioural skills, and are often not invited to social activities by their peers.¹⁹

Dealing with children with ADHD is very challenging for parents, who are left with little time to themselves, and family relationships can be severely affected.¹⁶ Furthermore, the presence of ADHD in children is associated with reduced parenting self-efficacy, lower

his document is protected by international copyright laws. No additional reproduction is authorized. It is permitted for personal use to download and save only one file and print only or copy of this Article. It is not permitted to make additional copies (either sparadically or systematically, either printed or electronic) of the Article for any purpose. It is not permitted to distribuhe electronic copy of the article through online internet and/or infranet file sharing systems, electronic mailing or any other means which may grow access to the Article. The use of all or ar

parental satisfaction and increased levels of parental stress, as indicated by several studies.²⁰⁻ ²³ Higher parenting stress levels characteristic of children with ADHD are clearly related to the child's disorder,²² but are also influenced by other factors such as parental practices, cognitions, problem-solving ability and family lifestyle.²⁴ Parents of children with ADHD may display lower family quality of life, less parental warmth, higher parental depression and anxiety, and more inconsistent and hostile parenting.²⁵

School holidays can be particularly demanding for parents of children with ADHD, especially if support from other family members is not available. However, the school period can also be very stressful for parents, due to the conflicts and difficulties children with ADHD encounter in the school setting²⁶ and consequent concerns about the child's ability to cope with the daily school routine.

The return to school after the summer holidays is a difficult time of year for all families and can generate mixed emotions in both parents and children. The back-to-school stress survey²⁷ was designed to compare stress in parents of children with and without ADHD as children prepare to return to structured school days after the less structured days of the summer break, and to obtain a better understanding of the stresses suffered by parents of children with ADHD during this time.

Materials and methods

The survey was conducted online in France, Germany, Italy, the Netherlands, Spain, the UK and Canada in September 2011. Written informed consent and ethics committee approval were not required as the survey was conducted as market research. Here, we analyse the results obtained in Italy and evaluate them in relation to combined data from the other

his document is protected by international copyright laws. No additional reproduction is authorized. It is permitted for personal use to download and save only one fle and print only or copy of this Artice. It is not permitted to make additional copies (either sporadically or systematically, either printed or electronic) of the Article for any purpose. It is not permitted to distribut ne electronic copy of the writice through online internet and/or intranet file sharing systems, electronic maining or any other means which may allow access to the Article. The use of oll or an

participating European countries. A detailed description of the overall European results has been published previously.²⁷

Participants

As previously described,²⁷ parents of children/adolescents aged 6–17 years were recruited and surveyed by a consumer research organization (Ipsos MORI, London, UK) from preexisting online panels of market research volunteers. Parents of children/adolescents with ADHD and parents of children/adolescents without ADHD (control group) were surveyed in each participating country. Respondents were selected based on demographic information held on the panel (age, gender, presence of children in the household), screened to determine whether they had a child with ADHD in the household and assigned to the corresponding group. Diagnosis of ADHD and/or other conditions was self-reported by parents; other conditions were selected from a predefined list. Quality checks were performed by the consumer research organization to eliminate undesired survey behaviour and exclude unengaged respondents.²⁷

For families with >1 child with ADHD, data were collected for the eldest. As a nominal incentive to complete the survey, respondents received points that could be exchanged for shopping vouchers.

Survey

The design and development of the survey have been previously described.²⁷ Briefly, the survey questionnaire was created in English and translated into local languages. Questions were identical in all countries and all translations were validated by native speakers. The

his document is protected by international copyright laws. No additional reproduction is authorized. It is permitted for personal use to download and save only one file and print only or copy of this Article. It is not permitted to make additional copies (either sparadically or systematically, either printed or electronic) of the Article for any purpose. It is not permitted to distribuhe electronic copy of the article through online internet and/or intranet file sharing systems, electronic mailing or any other means which may of ow access to the Article. The use of all or or questionnaire included 28 questions regarding the demographics of participants and characteristics of children and their families, and stress-related questions that were rated by parents on a scale ranging from 1 (low stress) to 10 (high stress). Questions regarding standard stress-causing situations requiring adaptive or coping behaviour were based on the example of the social readjustment rating scale developed by Holmes and Rahe in 1967²⁸ and combined into four domains: personal life, family life, life events and events throughout the year. Questions evaluating stress-causing situations specifically related to the back-to-school period were combined into six domains: preparing for back-to-school, day-to-day school stresses, stresses regarding negative experiences for the child, parental stresses, interactions with school and teachers, and general stress of going back to school. Questions composing each domain have been published elsewhere.²⁷ Confidentiality was secured by allocating a number to any completed questionnaire filed via the internet and then deleting the respondent's email address.

Statistical analyses

Descriptive statistics were used to summarize the survey results. These included mean, standard deviation (SD), median, minimum and maximum values for continuous data, and counts and percentages for categorical data. Stress levels were evaluated by calculating total and mean stress scores, SDs and 95% confidence intervals for the mean for each domain. Exploratory testing using Student's *t*-test was performed to compare the ADHD and control groups.²⁷ Similarly, within-group comparisons of stress at different times of the year relative to the back-to-school period (paired differences) were performed using Student's *t*-test. No formal sample size calculations were performed; a minimum number of 100 respondents per group per country was considered to be a reasonably representative sample to detect differences between groups. As samples were relatively well matched demographically, no

his document is protected by international copyright laws. No additional reproduction is authorized. It is permitted for personal use to download and save only one file and print only or copy of this Article. It is not permitted to make additional copies (either sporadically or systematically, either printed or electronic) of the Article for any purpose. It is not permitted to distribut the electronic copy of the article through on ne internet and/or intranet file sharing systems, electronic maining or any other means which may allow access to the Article. The use of oll or ar covariate adjustment for demographic characteristics was done. For some questions, only the most frequent answers are reported and/or multiple answers were allowed; therefore, the total percentage of respondents does not always equal 100%.

Results

Demographics and background of participants

In Italy, 107 and 105 parents of children with and without ADHD, respectively, participated in the survey.

The demographics and background characteristics of Italian participants are shown in **Table I**. The ADHD and non-ADHD groups were generally similar, but the percentage of women was higher in the ADHD group (60.7% compared with 49.5% in the non-ADHD group). The ADHD group also showed a higher proportion of single (2.8% vs none) and divorced or separated parents (7.5% vs 4.8%) relative to the non-ADHD group. Similar differences between parents of children with and without ADHD were observed in the European sample; however, a higher percentage of respondents were part of a two-parent family in Italy (married or in a civil partnership, 81.3% in the ADHD group and 88.6% in the non-ADHD group) than in the European sample (65.0% and 74.1%, respectively). Most respondents in the ADHD group had only one child with ADHD (n=104, 97.2%).

With respect to the presence of ADHD within the family, approximately one fifth (n=23, 21.5%) of participants in the ADHD group reported that at least one family member other than the child had also been diagnosed with the disorder; in 34.8% (n=8) of these families the mother had ADHD, in another 34.8% (n=8) the father and in 39.1% (n=9) other relatives

were affected. In the European sample, the proportion of families in the ADHD group that had other affected members was slightly higher (27.3%).

The majority of Italian parents in the ADHD group (n=86, 80.4%) were receiving help to look after their child with ADHD, most frequently from the partner (n=56, 52.3%), the child's grandparents (n=43, 40.2%) or other family members (n=15, 14.0%). Receiving support from the grandparents was more common in Italy than in the other European countries (27.3%).

Characteristics of children with ADHD

The characteristics of children with ADHD in the Italian sample versus the other European countries (combined data) are presented in **Table II**. The two samples were generally similar, although Italian children were slightly younger than their European counterparts.

Schooling patterns were comparable between Italy and Europe, the main difference being that a higher proportion of children in Italy were starting school for the first time (12.1% vs 3.6%). In both samples, approximately 40% of children were receiving specialist support at school. Some differences were observed in school travel patterns between samples. In Italy, over half of children (55.1%) travelled to school by car, compared with 31.3% in Europe. Of those children who used public transport or walked to school, 50.9% did so under adult supervision in Italy, versus 35.5% in Europe; 49.1% went to school with other peers, siblings or friends, versus 32.1% in the European sample, and only 18.2% went on their own, versus 39.9%.

The use of ADHD medication was lower in Italy compared with the other European countries, with 32.7% and 53.3% of children receiving pharmacological treatment, respectively (**Table II**). In both settings, it was common practice to take a medication break during the summer holidays (approximately 40% of cases). In Italy, this was suggested mainly by the physician (n=11, 78.6%) and less frequently (n=3, 21.4%) by the parents themselves, while in Europe, medication breaks were less frequently suggested by the doctor (n=56, 49.6%). The majority (71.4%) of children who interrupted their medication restarted it >2 weeks before returning to school in Italy, compared with 0–2 weeks in Europe (90.3%).

Information provided by parents indicated that the diagnosis of comorbid conditions was more common in Italy than in Europe; in fact, 72.9% versus 59.4% of children with ADHD had at least one comorbidity in the two settings, respectively (**Table III**). Individual comorbid conditions in children with ADHD were more common in the Italian than in the European sample, with the exception of autism spectrum disorder (7.5% in Italy and 13.9% in Europe) and obsessive compulsive disorder (2.8% and 3.0%). Notable differences between the two samples were observed for conduct disorder (24.3% in Italy and 13.9% in Europe), early speech/communication problems/language disorder (19.6% and 11.3%), anxiety (14.0% and 8.9%), epilepsy (11.2% and 2.6%) and tics (8.4 and 4.0). Diagnosed conditions in children without ADHD were slightly more common in the European than the Italian sample and were generally lower than in the ADHD group (**Table III**). Children with ADHD in the Italian sample had greater percentages of internalizing, externalizing, neurodevelopmental and non-neurodevelopmental disorders compared with the non-ADHD group (**Table IV**).

The majority of children in the ADHD group (n=75, 70.1%) had been involved in some form of structured activity over the summer holidays, such as a summer camp (n=50, 66.7%),

behavioural therapy (n=33, 44.0%), educational training (n=10, 13.3%) or other activities (n=2, 2.7%). The proportion of children participating in summer activities was noticeably lower in the European sample (34.3%).

Stress levels in parents of children with or without ADHD

The analysis of stress levels experienced by parents in the ADHD and non-ADHD groups in the Italian and European samples is shown in **Figure I**. Both in Italy and Europe, parents of children with ADHD showed higher stress levels than parents of children without ADHD in all domains.

In Italy, for the four standard domains, the differences between the ADHD and non-ADHD groups were all statistically significant (p<0.05), except for personal life (p=0.06). Significant differences (p \leq 0.005) were observed between parents of children with and without ADHD for all six domains specifically related to the back-to-school period. The differences between the mean stress scores reported by the two groups generally appeared more accentuated for the domains related to the return to school (difference range: 0.8-1.9 points) than for the standard domains (0.5-1.0). These results were similar to those obtained in the European sample, where statistical significance was reached for all domains (p<0.05).

Overall, parents in the Italian sample showed higher stress levels than parents in the European sample, both in the ADHD group and in the non-ADHD group. For parents of children with ADHD, mean stress scores across domains ranged from 4.9 to 7.3 in Italy, and from 3.6 to 6.8 in the other European countries, while for the non-ADHD groups ranges were 3.9–6.5 in Italy and 2.8–6.2 in Europe. In general, the differences between ADHD and non-ADHD groups were slightly more pronounced in the Italian sample; this was particularly

evident for preparing for back to school (difference between groups: 1.9 points in Italy and 0.9 in Europe) and general stress of going back to school (difference between groups: 1.6 and 1.1). Compared with the other participating countries considered individually, stress levels in the Italian ADHD group were highest in all areas except family life and general stress of going back to school, where Italy had the second highest score after the UK, and stresses regarding negative experiences for the child (third highest score after Spain and the UK).

An analysis of the individual items composing the events throughout the year domain (i.e. Christmas, Easter, summer holidays, return to school after a holiday/new school term, own birthday, child's birthday, and annual performance review at work) (**Figure II**) showed that, in both the Italian and European samples, stress was higher in the ADHD group than in the non-ADHD group for all events. In Italy, for both groups, the return to school was the most stressful time of the year (mean stress score: 6.0 in the ADHD group and 4.9 in the non-ADHD group) followed by an annual performance review at work (5.9 and 4.7) and Christmas (5.1 and 4.6). Within the ADHD group, the return to school was significantly more stressful (p<0.001) than any other event, with the exception of an annual performance review at work (data not shown); the same happened within the non-ADHD group, with the exception of an annual performance review and Christmas.

Discussion

As expected, Italian parents of children with ADHD reported higher levels of stress than parents of children without ADHD. This is consistent with the European results of the survey and with previous data on parenting stress in families of children with ADHD.²¹⁻²³ As observed in the European sample, the differences in stress levels between ADHD and non-ADHD groups appeared more pronounced for areas specifically related to the return to school

his document is protected by international copyright laws. No additional reproduction is authorized. It is permitted for personal use to download and save only one file and print only or copy of this Article. It is not permitted to make additional copies (either sporadically or systematically, either printed or electronic) of the Article for any purpose. It is not permitted to distribuhe electronic copy of the article through online internet and/or intranet file sharing systems, electronic maining or any other means which may glow access to the Article. The use of all or a

than for standard areas, which confirms that the back-to-school period can be particularly critical for parents of children with ADHD.

The results of this survey provide valuable, country-specific, socio-demographic information, which can be useful to identify particular population characteristics that may have an impact on parenting stress. For example, relative to European respondents, the Italian sample showed a lower proportion of divorced or separated parents, and the ADHD group reported greater involvement of grandparents in the life of children as well as a higher participation of children in structured summer activities. In contrast with these elements, which may intuitively reduce parental stress, there were others that may conversely increase it, such as greater adult supervision when children go to school and lower use of ADHD medication. Interestingly, the stress levels reported by Italian parents were generally higher than those reported by European parents, both in the ADHD and non-ADHD groups. The balance between positive factors that may protect against parental stress in the Italian setting and negative factors that may exacerbate it could explain these differences, along with the fact that Italian parents typically tend to be more apprehensive, vigilant and absorbed by their children's needs. The differences in the levels of stress between ADHD and non-ADHD groups were also slightly higher in the Italian sample, possibly due to social and cultural factors and variation in disease management between countries. As parenting behaviour has been shown to have an impact on the child's behaviour and can influence the presentation of ADHD symptoms,^{20, 29} these data highlight the importance of taking parental stress into consideration in order to manage ADHD comprehensively and effectively.

ADHD has high heritability;³⁰ in the present study, more than one-fifth of participants reported that at least one family member other than the child had also been diagnosed with

ADHD, over two-thirds of whom were the child's parents. It is likely that having ADHD themselves may further reduce a parent's ability to cope with their child's ADHD and increase parental stress levels.

Another aspect that it is important to highlight is the presence of comorbid disorders, which is an added complicating factor in children with ADHD. Our analysis showed differences in the prevalence of comorbid conditions between the Italian and the European samples, with a higher prevalence in Italy of anxiety, conduct disorder, communication and language disorders, and epilepsy, and a lower prevalence of autism spectrum disorder; conversely, the prevalence of oppositional defiant disorder was similar between the two samples. While the observed variation is likely to reflect differences in diagnostic patterns between the participating countries, it is important to consider that the higher prevalence of anxiety disorders in Italy may be related to a delay in the diagnosis of ADHD, due to cultural and policy reasons. At the present time in Italy, ADHD is largely under-recognized and undertreated.^{8, 31} Prompt diagnosis is important as, when left undiagnosed, ADHD frequently leads to a significantly increased risk for diverse mental health conditions, such as anxiety and depression.³² Additionally, a diagnostic delay may facilitate the development of secondary comorbid conditions, such as conduct disorder. It is of note that family functioning is more impaired when ADHD is associated with comorbid oppositional and conduct problems, which lead to greater stress within the family, higher rates of parental psychopathology and conflictive parent-child relationships.³³ Among the six European countries, Italy had the highest frequency of diagnosis of comorbid conditions; in Italy, over 70% of children had been diagnosed with least one disorder in addition to ADHD, while in the other countries the frequency of diagnosis ranged from 42.7% in Spain to 68.3% in France. Compared with the ADHD group, the prevalence of diagnosed conditions in the non-ADHD group was low and was slightly greater in the European than the Italian sample.

his document is protected by international copyright laws. No additional reproduction is authorized. It is permitted for personal use to downlock and save only one file and print only or copy of this Article. It is not permitted to make additional copies (either sporadically or systematically, either printed or electronic) of the Article for any purpose. It is not permitted to distributhe electronic copy of the article through online internet and/or intranet file sharing systems, electronic mailing or any other means which may allow access to the Article. The use of all or ar

Regarding the use of ADHD medication, only one third of children in Italy were receiving pharmacological treatment, compared with almost half in Europe. This is consistent with the Italian clinical guidelines for ADHD, which recommend psychoeducational interventions as first-line treatment,³⁴ and with the limited availability of pharmacological therapeutic options compared with other countries. Cultural factors also impact knowledge and beliefs regarding ADHD treatment, leading to reduced use of medication. In agreement with this cultural position, the percentage of doctors suggesting a medication break during the school holiday was higher in Italy than in Europe; although this is in accordance with prescribing information and current approaches to therapy, questions have been raised regarding the usefulness of treatment interruptions.³⁵ Our finding that the difference in stress levels between parents of children with and without ADHD was more pronounced in the Italian sample than in the European sample may be in part related to the lower use of ADHD medication in Italy.

This study has some limitations, which have previously been discussed, and the results should be interpreted with caution.²⁷ These include the indicative nature of the data as the questionnaire is not a validated measure of stress and rigorous statistical analysis was not performed, the diagnosis of ADHD and comorbidities was not confirmed by a physician, the distribution of participants across countries may be uneven, which may affect the validity of between-country comparisons, and that survey participants may represent a selected population of parents with knowledge of information technology and greater awareness of ADHD, which may limit the generalizability of the results. However, the similarity of the Italian and overall European results suggests that ADHD has an important impact on parental

his document is protected by international copyright laws. No additional reproduction is authorized. It is permitted for personal use to downlock and save only one file and print only or sopy of this Article. It is not permitted to make additional copies (either sporadically or systematically, either printed or electronic) of the Article for any purpose. It is not permitted to distribut the electronic copy of the article through on the internet and/or intranet file sharing systems, electronic mathematically or any other means which may allow access to the Article. The use of all or ar

stress, in particular during the back-to-school period, regardless of social and cultural differences between countries.

Conclusions

The results of the back-to-school survey in Italy show that, as in other countries, ADHD is associated with increased parental stress, which becomes more apparent when children prepare to return to school. Although the limitations of the survey should be considered, these data highlight the importance of using a comprehensive approach and considering parenting stress in addition to the child's characteristics when diagnosing ADHD and comorbid disorders, as parenting behaviour can affect and exacerbate the child's symptoms. The information obtained from the survey can be useful to design psychosocial programmes to better support parents of children with ADHD, helping them to manage their stress and deal with their children more effectively and taking into account the unique characteristics of the Italian setting.

his document is protected by international copyright laws. No additional reproduction is authorized. It is permitted for personal use to download and save only one file and print only or copy of this Article. It is not permitted to make additional copies (either sporadically or systematically, either printed or electronic) of the Article for any purpose. It is not permitted to distribut the electronic copy of the article through online internet and/or intranet file sharing systems, electronic maling or any other means which may allow access to the Article. The use of all or ar

References

Polanczyk G, Salum GA, Sugaya LS, Caye A, Rohde LA. Annual Research Review: A meta-analysis of the worldwide prevalence of mental disorders in children and adolescents., 56 ed 2015: 345-365.

- 2 Polanczyk G, de Lima MS, Horta BL, Biederman J, Rohde LA. The worldwide prevalence of ADHD: a systematic review and metaregression analysis. Am J Psychiatry 2007;164:942-8.
- 3 American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders, Fourth edition, Text Revision. Washington, DC: APA; 2000.
- 4 World Health Organization. International Classification of Diseases (ICD-10). Geneva, Switzerland: WHO; 1992.
- 5 Taurines R, Schmitt J, Renner T, Conner AC, Warnke A, Romanos M. Developmental comorbidity in attention-deficit/hyperactivity disorder. Atten Defic Hyperact Disord 2010;2:267-89.
- 6 Faraone S, Pucci M, Coghill D. Pharmacotherapy for attention-deifcit-hyperactivity disorder. Eur Psychiatric Rev 2008;2:44-9.
- 7 Istituto Superiore di Sanità. ADHD. 2012. Available from: <u>http://www.iss.it/adhd/index.php?lang=1</u>
- 8 Didoni A, Sequi M, Panei P, Bonati M. One-year prospective follow-up of pharmacological treatment in children with attention-deficit/hyperactivity disorder. Eur J Clin Pharmacol 2011;67:1061-7.
- 9 Frigerio A, Rucci P, Goodman R, Ammaniti M, Carlet O, Cavolina P *et al.* Prevalence and correlates of mental disorders among adolescents in Italy: the PrISMA study. Eur Child Adolesc Psychiatry 2009;18:217-26.
- 10 Faravelli C, Lo SC, Castellini G, Ricca V, Pallanti S. Prevalence and correlates of mental disorders in a school-survey sample. Clin Pract Epidemiol Ment Health 2009;5:1-8.
- 11 Bianchini R, Postorino V, Grasso R, Santoro B, Migliore S, Burlo C *et al.* Prevalence of ADHD in a sample of Italian students: A population-based study. Research in Developmental Disabilities 2013;34:2543-50.
- 12 NICE. Attention deficit hyperactivity disorder. Diagnosis and management of ADHD in children, young people and adults. Leicester; London: The British Psychological Society; The Royal College of Psychiatrists, 2009.
- 13 Taylor E, Dopfner M, Sergeant J, Asherson P, Banaschewski T, Buitelaar J et al. European clinical guidelines for hyperkinetic disorder -- first upgrade. Eur Child Adolesc Psychiatry 2004;13 Suppl 1:i7-i30.
- 14 Istituto Superiore di Sanità. Registro nazionale dell'ADHD. 2012. Available from: http://www.iss.it/regi/cont.php?id=104&tipo=45&lang=1.
- 15 Curatolo P, D'Agati E, Moavero R. The neurobiological basis of ADHD. Ital J Pediatr 2010;36:79.
- 16 Harpin VA. The effect of ADHD on the life of an individual, their family, and community from preschool to adult life. Arch Dis Child 2005;90(Suppl 1):i2-i7.
- 17 Biederman J, Petty CR, Fried R, Kaiser R, Dolan CR, Schoenfeld S *et al.* Educational and occupational underattainment in adults with attention-deficit/hyperactivity disorder: a controlled study. J Clin Psychiatry 2008;69:1217-22.
- 18 Mannuzza S, Klein RG, Bessler A, Malloy P, Hynes ME. Educational and occupational outcome of hyperactive boys grown up. J Am Acad Child Adolesc Psychiatry 1997;36:1222-7.

his document is protected by international copyright laws. No additional reproduction is authorized. It is permitted for personal use to download and save only one file and print only or copy of this Article. It is not permitted to make additional copies (either sportatically or systematically, either printed or electronic) of the Article for any purpose. It is not permitted to distribune electronic copy of the article through online internet and/or intranet file sharing systems, electronic run ing or any other means which may a ow access to the Article. The use of all or ar

- 19 Hoza B, Mrug S, Gerdes AC, Hinshaw SP, Bukowski WM, Gold JA *et al.* What aspects of peer relationships are impaired in children with attention-deficit/hyperactivity disorder? J Consult Clin Psychol 2005;73:411-23.
- 20 Johnston C, Mash EJ. Families of children with attention-deficit/hyperactivity disorder: review and recommendations for future research. Clin Child Fam Psychol Review 2001;4:183-207.
- 21 Graziano PA, McNamara JP, Geffken GR, Reid A. Severity of children's ADHD symptoms and parenting stress: a multiple mediation model of self-regulation. J Abnorm Child Psychol 2011;39:1073-83.
- 22 Pimentel MJ, Vieira-Santos S, Santos V, Vale MC. Mothers of children with attention deficit/hyperactivity disorder: relationship among parenting stress, parental practices and child behaviour. Atten Defic Hyperact Disord 2011;3:61-8.
- 23 Whalen CK, Odgers CL, Reed PL, Henker B. Dissecting daily distress in mothers of children with ADHD: an electronic diary study. J Fam Psychol 2011;25:402-11.
- 24 Tamm L, Holden GW, Nakonezny PA, Swart S, Hughes CW. Metaparenting: associations with parenting stress, child-rearing practices, and retention in parents of children at risk for ADHD. Atten Defic Hyperact Disord 2012;4:1-10.
- 25 Cussen A, Sciberras E, Ukoumunne OC, Efron D. Relationship between symptoms of attention-deficit/hyperactivity disorder and family functioning: a community-based study. Eur J Pediatr 2012;171:271-80.
- 26 Anastopoulos AD, Guevremont DC, Shelton TL, DuPaul GJ. Parenting stress among families of children with attention deficit hyperactivity disorder. J Abnorm Child Psychol 1992;20:503-20.
- 27 Hernandez-Otero I, Doddamani L, Dutray B, Gagliano A, Haertling F, Bloomfield R. Stress levels experienced by parents of children with and without attentiondeficit/hyperactivity disorder during the back-to-school period: results of a European and Canadian survey. Int J Psychiatry Clin Pract 2014; In press.
- 28 Holmes TH, Rahe RH. The Social Readjustment Rating Scale. J Psychosom Res 1967;11:213-8.
- 29 Shin HS, Kim JM. [Analysis of relationships between parenting stress, maternal depression, and behavioral problems in children at risk for Attention Deficit Hyperactive Disorder]. J Korean Acad Nurs 2010;40:453-61.
- 30 Faraone SV, Perlis RH, Doyle AE, Smoller JW, Goralnick JJ, Holmgren MA et al. Molecular genetics of attention-deficit/hyperactivity disorder. Biol Psychiatry 2005;57:1313-23.
- 31 Hodgkins P, Setyawan J, Mitra D, Davis K, Quintero J, Fridman M *et al.* Management of ADHD in children across Europe: patient demographics, physician characteristics, and treatment patterns. Eur J Pediatr 2013;172:895-906.
- 32 Berger I. Diagnosis of attention deficit hyperactivity disorder: much ado about something. Isr Med Assoc J 2011;13:571-4.
- 33 Deault LC. A systematic review of parenting in relation to the development of comorbidities and functional impairments in children with attentiondeficit/hyperactivity disorder (ADHD). Child Psychiatry Hum Dev 2010;41:168-92.
- 34 Societa' italiana di neuropsichiatria dell'infanzia e dell'adolescenza (SINPIA). Lineeguida per la diagnosi e la terapia farmacologica del Disturbo da Deficit Attentivo con Iperattività (ADHD) in età evolutiva. 2002. Available from: http://www.sinpia.eu/atom/allegato/149.pdf.
- 35 Spencer TJ, Faraone SV, Biederman J, Lerner M, Cooper KM, Zimmerman B. Does prolonged therapy with a long-acting stimulant suppress growth in children with ADHD? J Am Acad Child Adolesc Psychiatry 2006;45:527-37.

²⁰

his document is protected by international copyright laws. No additional reproduction is authorized. It is permitted for personal use to download ond save only one file and print on y or copy of this Article. It is not permitted to make additional copies (either sporadically or systematical'y, either printed or electronic) of the Article for any purpose. It is not permitted to distribuhe electronic copy of the article through online internet and/or intranet file sharing systems, electronic mailing or any other means which may allow access to the Article. The use of all or ar

Figure I. Stress levels in parents of children with and without ADHD in the Italian and European samples

Figure II. Stress levels at different times of the year in the Italian and European samples ADHD, attention-deficit/hyperactivity disorder

his document is protected by international copyright laws. No additional reproduction is authorized. It is permitted for personal use to download and save only one file and print ony or copy of this Article. It is not permitted to make additional copies (either sporadically or systematically, either printed or eactronic) of the Article for any purpose. It is not permitted to distributhe electronic copy of the article through online internet and/or intranet file sharing systems, electronic maring or any other means which may allow access to the Article. The use of all or ar

	ADHD group	non-ADHD group
	n=107	n=105
Mean age, years (SD)	40.3 (7.3)	42.2 (6.6)
Female, n (%)	65 (60.7)	52 (49.5)
Number of children at home, n (%)		
	45 (42.1)	68 (64.8)
2	50 (46.7)	32 (30.5)
>2	12 (11.2)	5 (4.8)
Marital status, n (%)		
Married/in a civil partnership	87 (81.3)	93 (88.6)
Living together	8 (7.5)	5 (4.8)
Single	3 (2.8)	0
Widowed	1 (0.9)	2 (1.9)
Divorced or separated	8 (7.5)	5 (4.8)
Parental/primary carer status, n (%)		
Parent/guardian and primary carer	94 (87.9)	83 (79.0)
Parent/guardian but not primary carer	12 (11.2)	22 (21.0)
Primary carer but not parent/guardian	1 (0.9)	0

Table I. Demographics and background characteristics of survey participants in Italy

ADHD, attention-deficit/hyperactivity disorder; SD, standard deviation.

his document is protected by international copyright laws. No additional reproduction is authorized. It is permitted for personal use to download and save only one file and print only or copy of this Article. It is not permitted to make additional copies (either sporadically or systematically, either printed or extronic) of the Article for any purpose. It is not permitted to distribune electronic copy of the unticle through online internet and/or infranet file sharing systems, electronic main gior any other means which may allow access to the Article. The use of oll or ar

Table II. Characteristics of children with ADHD in the Italian sample and in the other

 participating European countries (combined data)

	Italy	Europe
	(n=107)	(n=505)
Mean age (SD), years	10.3 (3.1)	11.4 (3.2)
Male	83 (77.6)	380 (75.2)
Schooling		
Starting school for the first time	13 (12.1)	18 (3.6)
Returning to school after a holiday	94 (87.9)	487 (96.4)
Attending primary school	57 (53.3)	232 (45.9)
Attending secondary school	50 (46.7)	273 (54.1)
Receiving specialist support at school	42 (39.3)	220 (43.6)
Medication		
Taking medication for ADHD	35 (32.7)	269 (53.3)
Interrupting treatment during the school holidays*	14 (40.0)	113 (42.0)
Restarting treatment 0–2 weeks before going back to school [†]	4 (28.6)	102 (90.3)
Restarting treatment >2 weeks before going back to school [†]	10 (71.4)	11 (9.7)

Unless stated otherwise, data are presented as numbers of children (%).

*n=35 for the Italian sample and 269 for the European sample; $\dagger n=14$ for the Italian sample and 113 for the European sample.

ADHD, attention-deficit/hyperactivity disorder; SD, standard deviation.

sorder

Table III. Comorbidities in children with ADHD and diagnosed conditions in children

without ADHD in the Italian and European samples

	ADHD group, n (%)		Non-ADHD group, n (%)	
-	Italian	European	Italian sample	European
Diagnosis	sample	sample	(n=105)	sample
	(n=107)	(n=505)		(n=588)
Conduct disorder	26 (24.3)	70 (13.9)	0	7 (1.2)
Learning disorder/dyslexia	25 (23.4)	105 (20.8)	3 (2.9)	28 (4.8)
Early speech/communication	21 (19.6)	57 (11.3)	3 (2.9)	37 (6.3)
problems/language disorder				
Anxiety	15 (14.0)	45 (8.9)	1 (1.0)	22 (3.7)
Coordination difficulties	14 (13.1)	41 (8.1)	1 (1.0)	15 (2.6)
Epilepsy	12 (11.2)	13 (2.6)	0	5 (0.9)
Oppositional defiant disorder	11 (10.3)	39 (7.7)	0	4 (0.7)
Tics	9 (8.4)	20 (4.0)	0	5 (0.9)
Autism spectrum disorder	8 (7.5)	70 (13.9)	0	9 (1.5)
Depression	6 (5.6)	19 (3.8)	0	2 (0.3)
Sensory integration disorder	5 (4.7)	12 (2.4)	0	3 (0.5)
Manic depressive disorder	3 (2.8)	5 (1.0)	0	0
Tourette syndrome	3 (2.8)	7 (1.4)	0	2 (0.3)
Obsessive compulsive	2(2.9)	15 (2 0)	0	0
disorder	3 (2.8)	15 (5.0)	0	0
Bipolar disorder	1 (0.9)	2 (0.4)	0	0
None	29 (27.1)	205 (40.6)	97 (92.4)	479 (81.5)

ADHD, attention-deficit/hyperactivity disorder.

his document is protected by international copyright laws. No additional reproduction is authorized. It is permitted for personal use to download and save only one file and print ony of this Article. It is not permitted to make additional copies (either sporadically or systematically, either printed or electronic) of the Article for any purpose. It is not permitted to distribut he electronic copy of the article through online internet and/or intranet file sharing systems, electronic right or any other means which may allow access to the Article. The use of all or an

Table IV. Number of children (%) with internalizing/externalizing disorders and

 neurodevelopmental/non-neurodevelopmental disorders in the Italian sample

	Italian sample		
	ADHD group	non-ADHD group	
	(n=107)	(n=105)	
Internalizing disorders	45 (42.1)	7 (6.7)	
Externalizing disorders	35 (32.7)	1 (1.0)	
No internalizing or externalizing disorders	51 (47.7)	97 (92.4)	
Neurodevelopmental disorders	40 (37.4)	6 (5.7)	
Non-neurodevelopmental disorders	28 (26.2)	1 (1.0)	
No neurodevelopmental or non-	58 (54.2)	98 (93.3)	
neurodevelopmental disorders			

ADHD, attention-deficit/hyperactivity disorder.

his document is protected by international copyright laws. No additional reproduction is authorized. It is permitted for personal use to download and save only one file and print only or copy of this Article. It is not permitted to make additional copies (either sporadically or systematically, either printed or electronic) of the Article for any purpose. It is not permitted to distribut he electronic copy of the article through online internet and/or intranet file sharing systems, electronic maring or any other means which may allow access to the Article. The use of all or all



Italian ADHD group (n=107) 🗌 Italian non-ADHD group (n=105) 🗌 European ADHD group (n=506) 🗌 European non-ADHD group (n=588)

*p<0.05; **p≤0.005; ***p≤0.001.

^an=498; ^bn=576; ^cn=502; ^dn=579; ^en=500; ⁱn=583; ^on=103; ^bn=501; ⁱn=581; ⁱn=578.

Mean score = mean of non-missing scores per participant.

ADHD, attention deficit hyperactivity disorder: SD, standard deviation.

This document is protected by international corporation laws. No additional reproduction is authorized. It is permitted for parsonal use to download and save only one file and print only and only of this Article. It is not permitted to make additional copies (either productly or systematicat), either printed or electronic of the Article for any purvoke. It is not nermitted to databate the electronic copy of the article through origine internet additional copies (either particular copy of the article for any various copy and the article for any purvoke. The valid of or any the electronic copy of the article through origine internet additional softeness, electronic mating or any other means which may additional copies to the article for any the softeness of the article.



Italian ADHD group (n=107) 🗌 Italian non-ADHD group (n=105) 🗌 European ADHD group (n=506) 🗌 European non-ADHD group (n=588)

*p<0.05; **p<0.005; ***p<0.001 °n=104; °n=103; °n=499; °n=578; °n=495; 'n=576; °n=106; °n=581; 'n=498; 'n=577; *n=500; 'n=579; "n=105; °n=582; °n=101; Pn=97; °n=445; 'n=536.

ORIGINAL RESEARCH

Evaluation of acute cardiovascular effects of immediate-release methylphenidate in children and adolescents with attention-deficit hyperactivity disorder

Marco Lamberti^{1,2} Domenico Italiano² Laura Guerriero¹ Gessica D'Amico³ Rosamaria Siracusano^{1,4} Massimo Ingrassia⁵ Eva Germanò¹ Maria Pia Calabrò³ Edoardo Spina² Antonella Gagliano¹

¹Division of Child Neurology and Psychiatry, Department of Pediatrics, ²Department of Clinical and Experimental Medicine, ³Division of Pediatric Cardiology, Department of Pediatrics, University of Messina, Messina, Italy; ⁴Institution of Clinical Physiology, CNR, Pisa, ⁵Division of Psychology, Department of Humanities and Social Sciences, University of Messina, Messina, Italy

Correspondence: Marco Lamberti Division of Child Neurology and Psychiatry, Department of Pediatrics and Department of Clinical and Experimental Medicine, Policlinico Universitario G. Martino, Via Consolare Valeria I, 98125 Messina, Italy Tel +39 090 221 2910 Fax +39 090 293 0414 Email mlamberti@unime.it; marcolb@ yahoo.it

submit your manuscript | www.dovepress.com Dovepress http://dx.doi.org/10.2147/NDT.S79866 Abstract: Attention-deficit hyperactivity disorder is a frequent condition in children and often extends into adulthood. Use of immediate-release methylphenidate (MPH) has raised concerns about potential cardiovascular adverse effects within a few hours after administration. This study was carried out to investigate acute effects of MPH on electrocardiogram (ECG) in a pediatric population. A total of 54 consecutive patients with attention-deficit hyperactivity disorder (51 males and 3 females; mean age =12.14±2.6 years, range 6-19 years), receiving a new prescription of MPH, underwent a standard ECG 2 hours before and after the administration of MPH 10 mg per os. Basal and posttreatment ECG parameters, including mean QT (QT interval when corrected for heart rate [QTc]), QTc dispersion (QTd) interval duration, T-peak to T-end (TpTe) intervals, and TpTe/OT ratio were compared. Significant modifications of both OTc and OTd values were not found after drug administration. QTd fluctuated slightly from 25.7±9.3 milliseconds to 25.1±8.4 milliseconds; QTc varied from 407.6±12.4 milliseconds to 409.8±12.7 milliseconds. A significant variation in blood pressure (systolic blood pressure 105.4 ± 10.3 vs 109.6 ± 11.5 ; P < 0.05; diastolic blood pressure 59.2±7.1 vs 63.1±7.9; P < 0.05) was observed, but all the data were within normal range. Heart rate moved from 80.5±15.5 bpm to 87.7±18.8 bpm. No change in TpTe values was found, but a statistically significant increase in TpTe/QTc intervals was found with respect to basal values (0.207±0.02 milliseconds vs 0.214±0.02 milliseconds; P < 0.01). The findings of this study show no significant changes in ECG parameters. TpTe values can be an additional parameter to evaluate borderline cases.

Keywords: ADHD, methylphenidate, cardiovascular effects, children, adolescents

Introduction

Attention-deficit hyperactivity disorder (ADHD) is a common behavioral disorder characterized by symptoms of inattention, impulsivity, and hyperactivity that impact several domains of the life of patients, their family, and society.^{1,2} Patients with untreated ADHD are associated with poorer long-term self-esteem and social functioning outcomes than no-ADHD controls.^{3,4}

Treatments and interventions for ADHD are different and include psychological therapies and pharmacological treatment, especially for severe clinical cases. Stimulants, such as amphetamines and methylphenidate (MPH), represent the mainstay of pharmacological treatment for ADHD.⁵ Amphetamines act by increasing presynaptic release of dopamine and other biogenic amines in the brain while MPH, a substituted phenethylamine, inhibits the reuptake of dopamine and norepinephrine and therefore its pharmacology is identical to that of amphetamines.⁶

© 2015 Lamberti et al. This work is published by Dove Medical Press Limited, and Licensed under Creative Commons Attribution — Non Commercial (unported, v3.0) permission from Dove Medical Press Limited, provided the work is properly attributed. Permissions by ond the scope of the License are administered by Dove Medical Press Limited, and the work is properly attributed. Permissions by the function on how to request permission may be found at: http://www.dovepress.com/permissions.php

There is strong evidence that MPH is effective in treating ADHD, but recently, concerns have increasingly been raised about the adverse effects of this drug. In the last few years, several studies about the cardiovascular safety of stimulant medications were carried out.7-12 Stimulants and MPH increase blood pressure (BP) and heart rate (HR) in patients with ADHD,13-17 although these cardiovascular effects do not seem to be severe.¹⁸⁻²⁰ Nevertheless, most evidence is based on clinical reports from small populations, so it remains controversial whether the use of stimulants is potentially associated with serious adverse cardiovascular events or otherwise. A recent nationwide prospective cohort study suggests that cardiovascular events are rare in children and adolescents but twice as likely in stimulant users as in nonusers with a complex, time- and dose-dependent relationship between cardiovascular adverse events and stimulant treatment.²¹

Stimulant drugs can be proarrhythmogenic because they are closely related to sympathomimetic amines. The autonomic nervous system plays an important role in sudden cardiac death (SCD). However, it is hard to establish a strict connection between drugs and sudden cardiac arrest in children and adolescents because SCD is a very rare event in pediatric populations. It is likely that significant changes of HR variability reflect diminished vagal tone and represent one of the key factors leading to SCD in adults.⁷ A pilot study by Buchhorn et al reports an improvement of HR variability in children under stimulant medication.¹⁶ The authors assume that this effect may be an important predictor of cardiovascular risk.

Drug-induced SCD is most commonly caused by torsades de pointes, a potentially life-threatening, polymorphic, ventricular tachycardia often associated with a QT interval prolongation. In clinical practice, several drugs are able to induce QT/QT interval when corrected for HR (QTc), prolongation and torsades de pointes.²² QT interval monitoring (QTc) is widely used as a predictor of fatal arrhythmias.²³ The QTc dispersion (QTd), a measure of the interlead variation in the QT, is believed to be a more reliable predictor for cardiovascular mortality in the general population. A QTc interval greater than 500 milliseconds, or a QTd greater than 100 milliseconds, is considered a risk factor for fatal arrhythmias.24 More recent studies indicate that prolongation of the interval between the peak and the end of the T wave (T-peak to T-end [TpTe]) on the 12-lead electrocardiogram (ECG) can represent a new marker of ventricular arrhythmogenesis. In fact, prolongation of the TpTe interval, measured in lead V5, is considered independently associated with SCD, and it can be a suitable risk indicator even when

the QTc is within range or not measurable due to prolonged QRS duration. 25,26

To date, the studies investigating the cardiovascular risk of immediate-release methylphenidate (IR-MPH) have exclusively considered the QTc and QTd variations.²⁷ TpTe and TpTe/QT intervals, along with QTc and QTd modifications have not been investigated in the context of ADHD and drug-related cardiovascular adverse effects. We therefore performed an observational prospective study aimed at examining the modifying effect of IR-MPH on the cardiovascular system in pediatric patients diagnosed with ADHD, in particular by measuring the acute effects of IR-MPH on the ventricular repolarization through TpTe and TpTe/QT intervals, along with QTc and QTd.

Experimental procedures Study population

Children and adolescent patients (mean age =12.14±2.6 years, range 6-19 years) were enrolled into this observational, prospective study to assess the arrhythmic risk of IR-MPH. Patients were considered eligible for the study if they were drug-naïve ADHD outpatients, had ADHD diagnosed according to Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5) criteria,²⁸ were attending the Unit of Child Neurology and Psychiatry of the University Policlinic of Messina between September 2013 and March 2014, and were new users of IR-MPH. None of the included patients had a history and signs or symptoms of cardiovascular, pulmonary, or endocrine disorders. The study was approved by the local ethics committee. Subjects and parents received detailed information about characteristics, potential adverse effects, and different treatment options for ADHD. All parents gave their written informed consent, and all the patients, when able, gave their consent as well.

Study design

In all enrolled patients, IR-MPH was started at an initial dosage of 5 mg/day and progressively titrated over 4 weeks until the therapeutic dose was achieved. The low and medium doses were 10 mg and 30 mg, respectively, for each child according to his/her weight. The high dose was 60 mg reached by only three adolescents. All patients in the study had body weight higher than 17 kg, and therefore, the range of dose administered was between 0.68 mg/kg body weight and 0.87 mg/kg body weight. Each treatment condition was administered 7 days, twice or three times daily, at breakfast (approximately 7.30 am), at lunch (approximately 12.30 pm), and in some cases, early afternoon (approximately 3.30 pm).
For each patient, two standard 12-lead ECGs were obtained at a paper speed of 25 mm/second with the same instrument (Cardioline delta 3 plus), on the same day and under similar conditions. The first (predose) ECG examination was performed before the administration of the first daily dose of IR-MPH; the second (postdose) ECG was executed 2 hours after drug intake, simultaneously with the serum peak of MPH.²⁹ Predose ECG was executed at least 16 hours after the administration of the last MPH dose on the previous day; therefore, MPH serum concentrations were minimal at the time of the examination. The duration of QT intervals was measured manually, by an experienced cardiologist, in all leads in which the onset of the QRS complex and the return of T wave to baseline were clearly identified. The QT duration was corrected for HR according to the Bazett's formula to produce QTc and averaged for all assessed leads (mean QTc). If respiratory sinus arrhythmia was present, the QT interval was measured in all leads where RR intervals were almost equal. TpTe interval was measured from the peak of the T wave to the end of T wave in lead V5.26 The TpTe/QT ratio was calculated as the ratio of TpTe in that lead to the corresponding QT interval.^{25,30,31} HR, RR, PR, and QRS intervals were also measured. QTd was calculated as the difference between the longest and shortest individual lead QTc. QTc intervals >450 milliseconds or 60 milliseconds longer than at baseline and QTd >100 milliseconds were considered abnormal.32,33 Normal values for TpTe interval and for TpTe/QT ratio, calculated on V5 leads, were ranged from 4 milliseconds to 100 milliseconds (mean 63.3±11.38 milliseconds, median 60 milliseconds) and from 0.12 to 0.29 (mean 0.195±0.0344, median 0.188), respectively.²⁵ Basal and 2-hour postintake ECG parameters, including QTc, QTd, and TpTe ratio interval duration, were compared.

Statistical analysis

The baseline and 2-hour postintake ECG parameters were presented as mean \pm standard deviation. Ranges

were also presented for the respective measurements. The baseline/posttreatment measures were compared using the paired-samples, two-sided *t*-test. Statistical significance was accepted at a P < 0.05 level. Data analyses were performed using SPSS[®] for Windows[®] package.

Results

A total of 54 subjects completed the study (51 males and 3 females, mean age 12.14 ± 2.6 years, range 6-19 years). Therapeutic dosages were obtained within a month after the beginning of MPH treatment, in all enrolled patients. The average final dose of IR-MPH was 18.5 mg/day, administered in two to three divided doses (range 10-60 mg/day) according to clinical individual needs.

Electrocardiographic changes

The mean, standard deviation, ranges, t, P, and d values of the ECG measurements before and 2 hours postintake of IR-MPH are shown in Table 1. No abnormal findings were observed in the ECG results at both times, including any changes in voltages, axes, or morphology. Moreover, there was no significant difference noted in QTc and QTd intervals between baseline and 2-hour postintake determination. No patient exhibited a QTc interval greater than 500 milliseconds or a QTd greater than 100 milliseconds, at both determinations. However, in all patients, a significant variation in BP (systolic BP 105.4±10.3 vs 109.6±11.5; P<0.05; diastolic BP 59.2±7.1 vs 63.1±7.8; P<0.05), as well as in HR values (80.5±15.5 bpm vs 87.7±18.4 bpm), was observed between baseline and 2-hour postintake values. No change in TpTe values was found (Table 2), but a statistically significant increase in TpTe/ QTc ratio was found with respect to basal values (0.207 ± 0.02) milliseconds vs 0.214 ± 0.02 milliseconds; P < 0.01).

Discussion

Our data suggest a relative cardiovascular safety of IR-MPH used to treat ADHD. In our patients, the administration

Table I	Comparison of	pre-MPH and 2-hour	post-MPH electrocardiogram	measurements

		0			
	Pre-MPH	2-hour post-MPH	t (df)	Р	Cohen's D
Heart rate (bpm)	80.5±15.5 (55–135)	87.7±18.4 (55–165)	-5.139 (53)	<0.01	-0.43
Systolic BP (mmHg)	105.4±10.3 (85–131)	109.6±11.5 (90–135)	-2.563 (47)	< 0.05	-0.38
Diastolic BP (mmHg)	59.2±7.1 (48–78)	63.1±7.8 (48–82)	-3.324 (47)	<0.01	-0.53
QTc max (milliseconds)	420.5±12 (379–440)	420.8±12 (392–447)	-0.155 (53)	0.877 (NS)	-0.02
QTc min (milliseconds)	394.7±13 (358–420)	395.7±13.6 (362–426)	-0.601 (53)	0.55 (NS)	-0.07
QTc mean (milliseconds)	407.6±12.4 (377.5–430.6)	409.8±12.7 (376.7–436.2)	-1.773 (53)	0.082 (NS)	-0.17
QTd (milliseconds)	25.7±9.3 (4–45)	25.1±8.4 (5-40)	0.37 (53)	0.713 (NS)	0.07

Note: Data are mean \pm standard deviation (range).

Abbreviations: BP, blood pressure; MPH, methylphenidate; NS, not statistically significant; QTc, QT interval when corrected for heart rate; QTd, QTc dispersion.

	Pre-MPH	2-hour post-MPH	t (df)	P	Cohen's D
TpTe (milliseconds)	75.9±6.2 (56–88)	77.4±6.2 (56–88)	-1.483 (53)	0.144 (NS)	-0.24
TpTe/QTc	0.207±0.02 (0.140-0.235)	0.214±0.02 (0.156–0.253)	-2.732 (53)	<0.01	-0.35

Note: Data are mean \pm standard deviation (range).

Abbreviations: MPH, methylphenidate; NS, not statistically significant; QTc, QT interval when corrected for heart rate.

of a standard dosage of IR-MPH is not associated with a statistically significant increase of QTc and QTd values compared to baseline. Nevertheless, treatment with IR-MPH was associated with a slight increase of systolic and diastolic BP. However, no patient exhibited values of BP exceeding the normal range, suggesting that MPH resulted in no consistent or clinically meaningful, short-term BP changes. Furthermore, we did not find significant differences between the acquired TpTe interval measurements. Even if we reported a TpTe/QT ratio increase between basal and posttreatment values, this value was within the normal range.

Indeed, although cardiovascular safety of MPH has been extensively explored in adults, in the last decade, few studies investigated the safety of these drugs in pediatric patients. Even though recent studies focusing on long-term safety have been performed, to date, findings about the association between stimulant use and adverse cardiovascular outcomes are conflicting.^{20,21,34} A systematic review by Westover and Halm³⁵ found evidence that the statistical power of studies performed on children and adolescents is limited by the sample size, although the absolute risk of an event is low. Studies on adults found an increased risk for transient ischemic attack and sudden death/ventricular arrhythmia, which was more suggestive of a genuine safety issue. However, their interpretation was limited due to differences in population, cardiovascular outcome selection/ ascertainment, and methodology.³⁵ In a meta-analysis by Mick et al about the cardiovascular effects of various Central Nervous System (CNS) stimulants in adults with ADHD, based on data from 10 placebo-controlled trials conducted in a pooled sample of 2,665 adults, the use of stimulants, but not of placebo, was associated with a statistically significant increase in mean HR.17 These modifications are thought to be mediated by the sympathomimetic effects, as well as the central and peripheral catecholaminergic effects, of stimulant medications.^{36,37} Minor but statistically significant changes in systolic BP (3.3 mmHg), diastolic BP (1.5 mmHg), and HR (3.9 bpm) were observed over a 1-year period in a sample of 432 children with ADHD aged 6-13 years, participating in an open-label extension trial of MPH-osmotic-controlled

release oral delivery system, 18–54 mg.³⁸ However, findings from the majority of randomized, controlled, and open-label studies coincide in considering that changes in BP and HR most commonly occur during the initial titration phase.³⁹

At typical therapeutic doses, in all age groups, several studies confirmed that cardiovascular changes were minor or of negligible clinical significance.^{11,35,40-43} Apart from one study44 with possible methodological issues,45 available epidemiological studies have not shown a significant association between ADHD drugs use and serious cardiovascular events.⁴⁶ A recent large study⁴⁷ on 1,200,438 children and young adults between the ages of 2 years and 24 years found no evidence that use of current medications for ADHD was associated with an increased risk of severe cardiovascular events (SCD, acute myocardial infarction, and stroke). Nevertheless, possible underreporting and rare deaths with the initiation of the medication remain reasons for concern. Two other large studies^{41,48} performed on 443,198 adults and on 241,417 children (3-17 years of age), respectively, support the findings of Cooper et al⁴⁷ thus confirming that ADHD drug use is not associated with increased risk of severe cardiovascular events.

Our data further confirm the safety of MPH in pediatric population and provide one more cardiovascular parameter (TpTe), possibly useful to identify borderline cases. In fact, preexisting conditions and other interindividual differences may raise the risk of harmful adverse effects, which need to be investigated as carefully as possible, particularly with regard to cardiac sequelae.¹⁹ In a recent study, Shahani et al screened 691 ECGs of patients with ADHD during a 2-year period.⁴⁹ Differences in ECG parameters were compared in patients already on ADHD medications compared to those starting a new ADHD treatment, as well as in the stimulant vs nonstimulant drugs group. According to our data, these authors conclude that screening ECGs rarely resulted in management changes for patients taking or starting ADHD medications. In view of these negative studies, it is probably not useful to monitor ECG parameters during routine psychostimulant treatment of children and adolescents with ADHD, unless there are risk factors or comorbid cardiovascular abnormalities. When ECG parameters need to be monitored for information regarding the repolarization, TpTe

could be useful. TpTe is the result of the global distribution of the repolarization process. In a recent study, it was significantly and independently associated with increased odds of SCD in subjects with coronary artery disease. Thus, TpTe measurement may extend the value of repolarization beyond the QTc, particularly in situations where QTc is either normal or not valid due to prolongation of QRS duration. Prolonged TpTe has potential for enhancement of SCD risk stratification and warrants evaluation in additional, larger populations.²⁶ This new ECG marker can be very useful when patients have instead cardiological pathologies (such as hypertension, Brugada syndrome, or others)⁵⁰ or metabolic diseases (like diabetes) before starting psychiatric pharmacological treatment. In fact, normal values of TpTe/QT ratio are relatively narrow, so it can be easier to find patients with high risks of torsades de pointes.

The most important limitation of this study includes the lack of a long-term follow-up. A causal link between the drug and the cardiovascular outcomes could not be definitively confirmed, as observational studies allow the investigation of association rather than causality. Nevertheless, given that ECGs were recorded 2 hours before and after the administration of MPH, it is improbable that the outcomes observed were not due to drug exposure. More studies are needed to confirm the cardiovascular safety during long-term therapy.⁴³ Furthermore, the study design does not permit the investigation of a time- and dose-dependent relationship between cardiovascular adverse events and stimulant treatment in children and adolescents, even though this was not within the scope of the study.

Conclusion

This study underlines the relative cardiac safety of IR-MPH in childhood, even if stimulants may exert a cardiovascular effect on BP and HR. MPH-induced changes seem to be modest and comparable with changes in cardiovascular functioning associated with normal daily activities. Thus, there appears to be a wide margin of cardiovascular safety when MPH is taken orally in usual doses by hyperactive children. However, particular caution should be exercised by physicians in prescribing these drugs to patients with a genetic predisposition to arrhythmias. It might be useful to carry out an ECG examination in all patients starting MPH therapy.¹⁰ Additionally, both QTc and QTd should be measured in order to warrant a reliable assessment of druginduced QT prolongation. TpTe can be an additional useful parameter. In children with known cardiac disease, arrhythmia, or risk factors for cardiac disease, ADHD treatment should be undertaken in consultation with a medical specialist with competence in pediatric cardiology.^{23,40}

Disclosure

The authors report no conflicts of interest in this work.

References

- Klassen AF, Miller A, Fine S. Health-related quality of life in children and adolescents who have a diagnosis of attention-deficit/hyperactivity disorder. *Pediatrics*. 2004;114(5):e541–e547.
- Spencer TJ, Biederman J, Mick E. Attention-deficit/hyperactivity disorder: diagnosis, lifespan, comorbidities, and neurobiology. *J Pediatr Psychol.* 2007;32(6):631–642.
- 3. Harpin V, Mazzone L, Raynaud JP, Kahle J, Hodgkins P. Long-term outcomes of ADHD: a systematic review of self-esteem and social function. *J Atten Disord*. Epub 2013 May 22.
- Shaw M, Hodgkins P, Caci H, et al. A systematic review and analysis of long-term outcomes in attention deficit hyperactivity disorder: effects of treatment and non-treatment. *BMC Med.* 2012;10:99.
- Wolraich M, Brown L, Brown RT, et al; Subcommittee on Attention-Deficit/Hyperactivity Disorder; Steering Committee on Quality Improvement and Management. ADHD: clinical practice guideline for the diagnosis, evaluation, and treatment of attention-deficit/hyperactivity disorder in children and adolescents. *Pediatrics*. 2011;128(5): 1007–1022.
- Reddy DS. Current pharmacotherapy of attention deficit hyperactivity disorder. *Drugs Today (Barc)*. 2013;49(10):647–665.
- Buchhorn R, Conzelmann A, Willaschek C, Stork D, Taurines R, Renner TJ. Heart rate variability and methylphenidate in children with ADHD. *Atten Defic Hyperact Disord*. 2012;4(2):85–91.
- Faraone SV. Using meta-analysis to compare the efficacy of medications for attention-deficit/hyperactivity disorder in youths. *Pharm Ther*. 2009;34(12):678–694.
- Safer DJ. Relative cardiovascular safety of psychostimulants used to treat attention-deficit hyperactivity disorder. *J Child Adolesc Psychop*harmacol. 1992;2(4):279–290.
- Silva RR, Skimming JW, Muniz R. Cardiovascular safety of stimulant medications for pediatric attention-deficit hyperactivity disorder. *Clin Pediatr (Phila)*. 2010;49(9):840–851.
- Stiefel G, Besag FM. Cardiovascular effects of methylphenidate, amphetamines and atomoxetine in the treatment of attention-deficit hyperactivity disorder. *Drug Saf.* 2010;33(10):821–842.
- Winterstein AG, Gerhard T, Kubilis P, et al. Cardiovascular safety of central nervous system stimulants in children and adolescents: population based cohort study. *BMJ*. 2012;345:e4627.
- Findling RL, Short EJ, Manos MJ. Short-term cardiovascular effects of methylphenidate and adderall. *J Am Acad Child Adolesc Psychiatry*. 2001;40(5):525–529.
- Samuels JA, Franco K, Wan F, Sorof JM. Effect of stimulants on 24-h ambulatory blood pressure in children with ADHD: a double-blind, randomized, cross-over trial. *Pediatr Nephrol*. 2006;21(1):92–95.
- Arcieri R, Germinario EA, Bonati M, et al; Italian Attention-Deficit/ Hyperactivity Disorder Regional Reference Centers. Cardiovascular Measures in Children and Adolescents with Attention-Deficit/ Hyperactivity Disorder Who Are New Users of Methylphenidate and Atomoxetine. J Child Adolesc Psychopharmacol. 2012;22(6):423–431.
- Buchhorn R, Muller C, Willaschek C, Norozi K. How to predict the impact of methylphenidate on cardiovascular risk in children with attention deficit disorder: methylphenidate improves autonomic dysfunction in children with ADHD. *ISRN Pharmacol.* 2012;2012:170935.
- Mick E, McManus DD, Goldberg RJ. Meta-analysis of increased heart rate and blood pressure associated with CNS stimulant treatment of ADHD in adults. *Eur Neuropsychopharmacol.* 2013;23(6): 534–541.

- Graham J, Banaschewski T, Buitelaar J, et al; European Guidelines Group. European guidelines on managing adverse effects of medication for ADHD. *Eur Child Adolesc Psychiatry*. 2011;20(1):17–37.
- Graham J, Coghill D. Adverse effects of pharmacotherapies for attention-deficit hyperactivity disorder: epidemiology, prevention and management. *CNS Drugs*. 2008;22(3):213–237.
- Vitiello B, Elliott GR, Swanson JM, et al. Blood pressure and heart rate over 10 years in the multimodal treatment study of children with ADHD. *Am J Psychiatry*. 2012;169(2):167–177.
- Dalsgaard S, Kvist AP, Leckman JF, Nielsen HS, Simonsen M. Cardiovascular safety of stimulants in children with attention-deficit/ hyperactivity disorder: a nationwide prospective cohort study. *J Child Adolesc Psychopharmacol.* 2014;24(6):302–310.
- Roden DM. Drug-induced prolongation of the QT interval. N Engl J Med. 2004;350(10):1013–1022.
- 23. Berg A, Bratane E, Odland HH, Brudvik C, Rosland B, Hirth A. Kardiovaskulær risikovurdering ved bruk av AD/HD-medikamenter hos barner hos barn [Cardiovascular risk assessment for the use of ADHD drugs in children]. *Tidsskr Nor Laegeforen*. 2014;134(7):710–714. Norwegian
- Schwartz PJ, Moss AJ, Vincent GM, Crampton RS. Diagnostic criteria for the long QT syndrome. An update. *Circulation*. 1993;88(2): 782–784.
- Bieganowska K, Sawicka-Parobczyk M, Bieganowski M, Piskorski J. Tpeak-Tend interval in 12-lead electrocardiogram of healthy children and adolescents Tpeak-Tend interval in childhood. *Ann Noninvasive Electrocardiol*. 2013;18(4):344–351.
- Panikkath R, Reinier K, Uy-Evanado A, et al. Prolonged Tpeak-to-Tend interval on the resting ECG is associated with increased risk of sudden cardiac death. *Circ Arrhythm Electrophysiol*. 2011;4(4):441–447.
- Ilgenli TF, Congologlu A, Ozturk C, Turkbay T, Akpinar O, Kilicaslan F. Acute effect of methylphenidate on QT interval duration and dispersion in children with attention deficit hyperactivity disorder. *Adv Ther*. 2007;24(1):182–188.
- APA. In: APA, editor. *Diagnostic and Statistical Manual of Mental Disorders*. 5th ed. Arlington: American Psychiatric Publishing; 2013.
- Wargin W, Patrick K, Kilts C, et al. Pharmacokinetics of methylphenidate in man, rat and monkey. *J Pharmacol Exp Ther.* 1983;226(2): 382–386.
- Antzelevitch C, Sicouri S, Di Diego JM, et al. Does Tpeak-Tend provide an index of transmural dispersion of repolarization? *Heart Rhythm*. 2007;4:1114–1116. [author reply 1116–1119].
- Shimizu M, Ino H, Okeie K, et al. T-peak to T-end interval may be a better predictor of high-risk patients with hypertrophic cardiomyopathy associated with a cardiac troponin I mutation than QT dispersion. *Clin Cardiol.* 2002;25(7):335–339.
- 32. Correll CU, Harris J, Figen V, Kane JM, Manu P. Antipsychotic drug administration does not correlate with prolonged rate-corrected QT interval in children and adolescents: results from a nested case-control study. J Child Adolesc Psychopharmacol. 2011;21(4):365–368.
- Germanò E, Italiano D, Lamberti M, et al. ECG parameters in children and adolescents treated with aripiprazole and risperidone. *Prog Neuropsychopharmacol Biol Psychiatry*. 2014;51:23–27.
- Clavenna A, Bonati M. Safety of medicines used for ADHD in children: a review of published prospective clinical trials. *Arch Dis Child*. 2014;99(9):866–872.

Neuropsychiatric Disease and Treatment

Publish your work in this journal

Neuropsychiatric Disease and Treatment is an international, peerreviewed journal of clinical therapeutics and pharmacology focusing on concise rapid reporting of clinical or pre-clinical studies on a range of neuropsychiatric and neurological disorders. This journal is indexed on PubMed Central, the 'PsycINFO' database and CAS,

Submit your manuscript here: http://www.dovepress.com/neuropsychiatric-disease-and-treatment-journal

- Westover AN, Halm EA. Do prescription stimulants increase the risk of adverse cardiovascular events? A systematic review. *BMC Cardiovasc Disord*. 2012;12:41.
- Negrao BL, Crafford D, Viljoen M. The effect of sympathomimetic medication on cardiovascular functioning of children with attention-deficit/ hyperactivity disorder. *Cardiovasc J Afr.* 2009;20(5):296–299.
- Volkow ND, Wang GJ, Fowler JS, et al. Cardiovascular effects of methylphenidate in humans are associated with increases of dopamine in brain and of epinephrine in plasma. *Psychopharmacology (Berl)*. 2003;166(3):264–270.
- Wilens TE, Biederman J, Lerner M. Effects of once-daily osmoticrelease methylphenidate on blood pressure and heart rate in children with attention-deficit/hyperactivity disorder: results from a one-year follow-up study. *J Clin Psychopharmacol*. 2004;24(1):36–41.
- Hammerness P, Wilens T, Mick E, et al. Cardiovascular effects of longer-term, high-dose OROS methylphenidate in adolescents with attention deficit hyperactivity disorder. *J Pediatr*. 2009;155(1):84–89, 89.e81.
- 40. Cortese S, Holtmann M, Banaschewski T, et al; European ADHD Guidelines Group. Practitioner review: current best practice in the management of adverse events during treatment with ADHD medications in children and adolescents. *J Child Psychol Psychiatry*. 2013;54(3): 227–246.
- Habel LA, Cooper WO, Sox CM, et al. ADHD medications and risk of serious cardiovascular events in young and middle-aged adults. *JAMA*. 2011;306(24):2673–2683.
- Martinez-Raga J, Knecht C, Szerman N, Martinez MI. Risk of serious cardiovascular problems with medications for attention-deficit hyperactivity disorder. CNS Drugs. 2013;27(1):15–30.
- Awudu GA, Besag FM. Cardiovascular effects of methylphenidate, amphetamines and atomoxetine in the treatment of attention-deficit hyperactivity disorder: an update. *Drug Saf.* 2014;37(9):661–676.
- Gould MS, Walsh BT, Munfakh JL, et al. Sudden death and use of stimulant medications in youths. *Am J Psychiatry*. 2009;166(9):992–1001.
- Johnson MR. Increased risk of sudden death among youths and stimulant use: determining alternate potential factors. *Am J Psychiatry*. 2010;167:214. [author reply 214–215].
- 46. Hammerness PG, Perrin JM, Shelley-Abrahamson R, Wilens TE. Cardiovascular risk of stimulant treatment in pediatric attention-deficit/ hyperactivity disorder: update and clinical recommendations. J Am Acad Child Adolesc Psychiatry. 2011;50(10):978–990.
- Cooper WO, Habel LA, Sox CM, et al. ADHD drugs and serious cardiovascular events in children and young adults. *N Engl J Med.* 2011; 365(20):1896–1904.
- Schelleman H, Bilker WB, Strom BL, et al. Cardiovascular events and death in children exposed and unexposed to ADHD agents. *Pediatrics*. 2011;127(6):1102–1110.
- Shahani SA, Evans WN, Mayman GA, Thomas VC. Attention deficit hyperactivity disorder screening electrocardiograms: a communitybased perspective. *Pediatr Cardiol.* 2014;35(3):485–489.
- Karaagac K, Yontar OC, Tenekecioglu E, et al. Evaluation of Tp-Te interval and Tp-Te/QTc ratio in patients with coronary artery ectasia. *Int J Clin Exp Med.* 2014;7(9):2865–2870.

Dovepress

and is the official journal of The International Neuropsychiatric Association (INA). The manuscript management system is completely online and includes a very quick and fair peer-review system, which is all easy to use. Visit http://www.dovepress.com/testimonials.php to read read quotes from published authors.



BMJ 2015;350:h2168 doi: 10.1136/bmj.h2168 (Published 20 May 2015)

CrossMan click for update

CLINICAL REVIEW

Childhood attention-deficit/hyperactivity disorder

Nienke Verkuijl *specialty trainee*¹, Marian Perkins *consultant*², Mina Fazel *NIHR postdoctoral research fellow*¹ *consultant*³

¹Department of Psychiatry, University of Oxford, Oxford OX3 7JX, UK; ²Child and Adolescent Neuropsychiatry Service, Oxford Health NHS Foundation Trust, Oxford, UK; ³Children's Psychological Medicine, The Children's Hospital, Oxford University Hospitals NHS Trust, Oxford, UK

Attention-deficit/hyperactivity disorder (ADHD) is the second most common psychiatric disorder of childhood.¹ The 2010 Global Burden of Disease Study found that worldwide point prevalence rates of childhood ADHD were 2.2% in males and 0.7% in females.² However, the diagnosis rates of and treatment approaches to ADHD vary worldwide, which feeds some of the uncertainties that have become a hallmark of the management of ADHD.

ADHD presents with persistent and impairing symptoms of inattention, hyperactivity, and impulsivity. Children with ADHD can be negatively labelled or treated differently at school and at home, as they struggle to concentrate, sit still, and think before acting, which can make learning and functioning in a typical classroom environment challenging. Furthermore, social interactions can be difficult, leading to rejection by peers³ and an often strained relationship with parents.⁴ In combination, these factors can create secondary adversities, such as greater risk of poor school attainment and exclusion, misuse of substances, and involvement with the criminal justice system (fig 11).⁵⁻⁸

ADHD is a disorder that attracts considerable debate and controversy. Data indicate that in some areas overdiagnosis is a problem,⁹ with concerns about the misuse of psychostimulants raised within the healthcare profession and elsewhere. However, the negative impact of unrecognised and untreated symptoms of severe ADHD must not be underestimated for children and their families. Both behavioural interventions and drugs improve outcomes compared with no intervention, although the functioning of affected children in the long term remains below that of their age and demographically matched peers.⁷

This review aims to provide an evidence based overview of the assessment and management of ADHD for clinicians. We also discuss some of the driving factors that may be behind the conflicting picture produced in the academic literature and popular science about ADHD, although a comprehensive assessment of these issues is beyond the scope of this review.

What causes it?

ADHD is due to both heritable and non-heritable factors.¹⁰ Twin studies indicate a high heritability, of around 70-80%.¹¹ ADHD is associated with several genes, some of which are common to other psychiatric disorders¹²; the genes are linked to dopaminergic and serotonergic pathways. Further associations with ADHD include maternal alcohol and substance misuse during pregnancy, low birth weight, prematurity, nutritional deficiencies, exposure to environmental toxins, and early psychosocial adversity.¹⁰

What are the current debates and controversies surrounding ADHD?

The diagnosis and treatment of ADHD have caused debate in many arenas, including within health and education professions,¹³⁻¹⁵ the media, and the general public.¹⁶ Although the core symptoms of ADHD lie at one end of the normal distribution of behaviour, a major debate has taken place as to whether ADHD is actually a disorder, and, if it is a disorder, where the diagnostic cut-off lies.^{15 17} However, it is noted that a large body of family, twin, and adoption studies converge to show that ADHD is highly heritable.¹⁷ Twin studies have consistently shown that ADHD has a heritability of around 80% for monozygotic and 40% for dizygotic twins.^{10 18-20}

Some of the reasons for this conflicting picture include:

Variation in prevalence and treatment rates

The wide variation in reported global prevalence and treatment rates is of concern and has been described as precipitating a confidence crisis in psychiatric diagnosis.^{21 22} This variation was highlighted by two studies from the United States and United Kingdom; both explored parent reported ADHD diagnosis "ever" made. The US study reported a 42% increase in ADHD diagnoses from 2003-11, with 8.8% having a current diagnosis of ADHD.²³ The UK study reported a prevalence of 1.7%, with

Correspondence to: M Fazel mina.fazel@psych.ox.ac.uk

113

Extra material supplied by the author (see http://www.bmj.com/content/350/bmj.h2168?tab=related#datasupp)

Examples of standardised rating scales for ADHD and their psychometric properties

The bottom line

- ADHD is diagnosed in a child with persistent symptoms of inattention, hyperactivity, and impulsivity leading to impairment in multiple settings
- · Associated problems include conduct disorder, learning difficulties, and autism spectrum disorders
- Psychosocial interventions, such as parent training and classroom interventions, can have an important role in improving self esteem, engagement with the school curriculum, and relationships with family and peers
- Drugs can improve core symptoms, school performance, and peer relationships; choice and monitoring of treatment is best conducted
 in specialist clinics in collaboration with primary care
- The rates of diagnosis and prescriptions of drugs for the treatment of ADHD have increased sharply in certain parts of the world and
 need to be better understood

Sources and selection criteria

We searched PubMed for meta-analyses, systematic reviews, and randomised controlled trials on epidemiology and drug and non-drug treatments of ADHD published from January 2004 to December 2013 (and updated December 2014). We also read the national and international guidelines for ADHD by the National Institute for Health and Care Excellence, the European Guidelines for Hyperkinetic Disorders, the American Academy of Pediatrics, and the American Academy of Child and Adolescent Psychiatry. Further landmark studies were added, and we also sought additional expert opinion.

How patients were involved in the creation of this article

We sought accounts from children, adolescents, and young adults with ADHD and their parents on their experience of healthcare and include some of these accounts as part of this review to provide essential information on the perceptions of drugs and care. This review was changed as a result of child and parent feedback, with greater emphasis then placed on different treatments and more information given on different drugs, as these were common areas of uncertainty.

no evidence of an increase between 1999 and 2009.^{1 24} Overall, 6.1% of children in the US receive drugs for ADHD, in contrast with an estimated 0.8% in the UK.²⁵

Location

Over and under diagnosis and treatment in certain geographical and population groups are additional factors. This is illustrated by the Great Smoky Mountain longitudinal study in the US. To identify those with ADHD, 4500 children were screened and those with behavioural problems were interviewed and observed as well as parent and teacher reports collected. Overall, 3.4% of the children were found to have ADHD, although 7.3% were taking psychostimulants.⁹ Interestingly, children living below the poverty line were less than half as likely to receive drugs.

Cultural expectations of behaviour

Current diagnostic frameworks for ADHD inevitably leave a subjective element, determining the degree to which functioning is affected. There is therefore a "zone of ambiguity" affecting diagnosis.¹³ ¹⁴ The judgment made by parents, teachers, and clinicians is influenced by cultural expectations of children's behaviour.¹⁴ Recent debate has also raised the problem that psychostimulants in some countries or socioeconomic groups are being misused as cognitive enhancers for young people, for which there is some evidence in normal controls.²⁶⁻²⁸ The clinician's role is to identify those children with a history of functional impairment as a result of attentional difficulties who might best benefit from drug treatment, balancing the benefits and potential side effects of drugs.

Classification

The two different diagnostic classification systems, the *International Classification of Diseases* (ICD) and the *Diagnostic and Statistical Manual of Mental Disorders* (DSM), may contribute to the variation in prevalence rates. This is because they each use different terms and diagnostic criteria for ADHD. When the criteria change, as in the recent move from DSM-IV to DSM-5, the changes can make comparisons between

1 diagnostic classification s studies difficult.^{14 24 29} The DSM is used mainly in North America and is also used internationally for research, whereas the ICD-10 is mostly used in clinical contexts outside the USA. DSM-5 utilises the term "ADHD" and has made several changes to the classification of the disorder when compared to its predecessor, whereas the ICD-10 does not use ADHD but the term "hyperkinetic disorder," which is equivalent to severe ADHD. International efforts are attempting to unify the main diagnostic categories across these two classification systems.³⁰

Involvement of industry

Financial interests and constraints can contribute to the complex interplay of factors. The pharmaceutical industry is reported to have influenced the current diagnostic inflation.^{21 22} In addition, many researchers and patient support groups, as well as 37% of websites about ADHD, have received ADHD related grants from the pharmaceutical industry.^{31 32} In the USA, drugs for ADHD are heavily advertised, and pharmaceutical companies are allowed to advertise directly to potential consumers and teachers, which can also influence consumption rates.³³ Limited access to behavioural and psychological treatments may sway doctors and patients towards using drugs earlier in the ADHD management pathway. Furthermore, some health insurance policies require a diagnosis to be present for any reimbursement of treatment.¹⁴

Strength of the evidence base

There is a paucity of good quality experimental data on drug treatments from which to draw firm conclusions. This problem is not specific to ADHD and affects many decisions about drugs across child psychiatry, reflecting the difficulty in both securing funding and studying child populations under ideal experimental conditions.³⁴ Therefore areas that would benefit from a stronger evidence base include the natural progression of ADHD and numerous questions around drug treatments, including long term effects, those subgroups most likely to benefit from treatment, and longitudinal outcomes of those receiving drugs compared with other treatments.³⁵

Page 3 of 14

How is it assessed and diagnosed?

Making the diagnosis

Countries differ on their guidelines when stipulating who is allowed to make an ADHD diagnosis, with many countries, such as the USA and the Netherlands, having primary care physicians making the diagnosis, and other countries, such as the UK, having a paediatrician or child psychiatrist confirm a suspected diagnosis of ADHD.^{36 37}

The three core symptoms of ADHD are inattention, hyperactivity, and impulsivity. In combination these symptoms most often manifest as children struggling with schoolwork and being disorganised. Such children are often described as "constantly on the go" and have poor awareness of danger. Social interactions can be problematic because of the high level of activity, reduced awareness of others' space, impulsivity, and inability to sustain play or a conversation for longer than a few minutes. Children are susceptible to bullying or are easily encouraged to do "silly" things that get them into trouble. Parents, especially mothers, often feel blamed for their child's behaviour, which can lead either to a reluctance to approach a doctor for help or to an eagerness to seek a diagnosis.³⁸⁻⁴⁰ The children may overhear negative comments, such as being described as "the most difficult" or the "worst behaved," and this can potentially impact on self esteem (fig $2\Downarrow$).

It is important at this stage to rule out common disorders that can lead to similar presentations, such as problems with sleep, hearing, and vision. Behavioural problems should be of a severity to cause significant stress and disruption at home and in the classroom. If other causes are ruled out and the problems persist with moderate impairment, referral to specialist services for a diagnosis is recommended. Younger children, more commonly boys, can present with difficulties at school and, in extremis, school exclusion,⁶ whereas girls have more attentional difficulties and ADHD can often remain undiagnosed until later when academic demands become greater. A referral to secondary care will be greatly aided by additional multidisciplinary reports-for example, from professionals working within the education sector, such as teachers, educational psychologists, and pastoral support staff.^{36 41} Referral to a parenting course can be made for the parents of children aged less than 11 years awaiting specialist assessment. Professionals recommending a parenting course need to be mindful of implying that parents have poor parenting skills. They should instead stress that children with these difficulties often benefit from more intensive parenting.

Box 1 highlights the DSM-5 criteria for a diagnosis of ADHD. A thorough history and examination are essential to determine the correct diagnosis and assess commonly associated conditions and comorbidities (box 2).

In addition to questions on core symptoms using diagnostic criteria, the clinical interview should include:

- Presenting problems, history of difficulties, and current functioning. It should consider the children's experiences of their symptoms and include general questions around risk taking
- Pregnancy, birth history, and history of early neurodevelopment (milestones, language, attachment, sleep, feeding problems, early temperament, social-communication development)
- Medical history (tics, epilepsy, cardiac symptoms, gross and fine motor skills, vision, and hearing), drug history, and family medical history, especially cardiac, such as

sudden death below 40 years or death associated with exercise

• Assessment of the level of global impairment at school, at home, and in a social context (a well validated tool for this is the Children's Global Assessment Scale)⁵⁴

Standardised questionnaires are widely used in the assessment and management of ADHD (see table on thebmj.com). Psychometric assessments can be useful if learning or communication difficulties are present. Chromosomal analysis and functional brain imaging are not routinely recommended.

How is ADHD treated?

The management of children with ADHD has to take place within a full understanding of the severity of their current difficulties, their socio-emotional needs, family circumstances, and educational environment.^{36 47} In view of the lifelong trajectory of children with severe impairments, the role and timing of drugs at different ages will need to be considered. For example, children being managed with behavioural and family strategies may be additionally supported by the use of drugs at key periods of transition or other stressors. Importantly, the management of ADHD in some families can potentially be complicated by undiagnosed and untreated ADHD in the parents.²⁵ Many supports available to families increasingly lie within education, social services, and the voluntary sector or the community, as well as in the healthcare setting.

Although the broad framework of assessment across the globe is relatively consistent for ADHD, countries do vary in the degree to which psychosocial interventions are prioritised compared with drug interventions, for reasons described above. The ADHD guidelines in the UK, which are broadly similar to the European and US guidelines recommend parent training programmes and behavioural strategies.³⁶ For severe ADHD, it is recommended that drugs should be offered alongside psychosocial interventions in children who are 6 years and older.^{36 47}The recommended investigations when starting drugs are:

- Physical examination—a cardiac examination to exclude any obvious abnormalities. Baseline pulse, blood pressure, height, and weight should be recorded
- Tests—electrocardiography only if there is a medical or family history of serious cardiac disease, a history of sudden death in young family members, or abnormal findings on cardiac examination. Blood tests are not routinely recommended

Psychosocial interventions for ADHD

The evidence base for many psychosocial interventions such as parent training, social skills training, cognitive training, or specific classroom interventions is limited.⁵⁵⁻⁵⁹

Findings from a systematic review and meta-analysis in 2013 of randomised controlled trials of non-drug treatments for ADHD found no evidence for the efficacy of behavioural interventions involving children, parents, or teachers on core ADHD symptoms when using blinded assessors. There was evidence for a small but significant effect of behavioural interventions when studies used non-blinded assessors such as parents.⁵⁵

In considering the long term role of behavioural interventions compared with drugs, the Multimodal Treatment study of children with ADHD (MTA) is the largest randomised clinical trial, with eight years' follow-up.⁷ The behavioural treatment

CLINICAL REVIEW

Page 4 of 14

Box 1 DSM-5 diagnostic criteria for ADHD⁸⁷

Six or more symptoms from each category are required for a diagnosis Inattention

- Makes careless mistakes
- · Has difficulty sustaining attention in tasks or play activities
- · Does not seem to listen when spoken to directly
- · Does not follow through on instructions and fails to finish homework
- · Has trouble organising tasks and activities
- · Avoids tasks that require sustained mental effort
- Loses things necessary for tasks or activities
- · Easily distracted
- Forgetful

Hyperactivity and impulsivity

- · Fidgets with hands or feet or squirms in seat
- Leaves seat in situations where remaining seated is expected
- · Runs about or climbs excessively in situations where these are inappropriate
- Has difficulty playing or engaging in leisure activities quietly
- Talks excessively
- "On the go" or often acts as if "driven by a motor"
- Has difficulty waiting turns
- · Blurts out answers before a question has been completed
- · Interrupts or intrudes on others

Symptoms are

- · Present for at least six months
- Presenting before age 12 years (if ≥17 years, only five symptoms in each category are required for a diagnosis)
- Present in at least two settings (for example, at school, at home, with friends, or in other activities) and symptoms interfere with quality
 of social or school functioning
- · Maladaptive and inconsistent with developmental level
- · Cannot be better explained by another mental disorder

studied was extensive and included parent, child, and school based elements. The drug arm consisted of tightly titrated treatment regimens. After 14 months of treatment, core ADHD symptoms were better in the drug arm than both behavioural treatment and routine community care. The combined treatment of behavioural intervention and drugs did not yield significantly greater benefits, but provided some advantages for non-ADHD symptoms such as social interactions and internalising symptoms. After 14 months the study became a naturalistic observation. At 24 months (10 months after trial completion) those children who had received a combination of drugs and behavioural management needed significantly lower drug doses.⁶⁰ At the eight year follow-up, however, the treatment groups did not differ on measures, including school attainment, criminal arrests, admissions to hospital for psychiatric disorders, or other relevant outcomes.⁷ The strongest positive predictor of long term outcome was behavioural and sociodemographic advantage and having a good response to any treatment.

Psychosocial interventions have, however, been shown to play an important role in the longer term management and treatment of comorbidities associated with ADHD, which can lead to improved overall functioning of children by improving their self esteem and peer and family relationships and making it easier for them to access the school curriculum.⁵⁹

Parent training for ADHD

116

Many parents report benefits from parent training, although a meta-analysis and Cochrane review have highlighted how its evidence base remains poor.^{55 57} In the UK, however, NICE guidelines recommend it as a first line treatment for children aged 3 to 11 years.³⁶ Parent training, as for example in the New

Forest Parenting programme⁶¹ (ADHD focused) and the Incredible Years programme (broad behavioural focus), includes psycho-education and techniques for managing challenging behaviours.^{57 62} The training is usually group based and emphasises three areas⁶³:

Focus on making wanted behaviours explicit—This can be through praise and reward rather than through criticising unwanted behaviour, such as telling children to sit down instead of shouting at them to stop being naughty, and by ignoring screaming and tantrums. A more positive relationship can be promoted through activities such as play.

Making a clear set of rules for the family—The rules should be explicit, succinct, and consistently enforced by parents. Disobedience and aggression need to be firmly and calmly dealt with—for example, by temporarily removing children from a situation.

Anticipating potentially difficult times of the day—In the context of busy family life, this entails proactively placing structure, distraction, or different activities at these times—for example, during key transitions, such as when returning home from school.

Social skills training

Social skills training includes learning appropriate verbal and non-verbal communication in social situations, understanding how to share and take turns, listening, and recognising other people's emotions. A recent Cochrane review on social skills training for children aged 5-18 years with ADHD found no evidence for or against this type of training.⁵⁶ This may be because the deficit in children with ADHD is not in their social

Page 5 of 14

Box 2 Comorbidities and associated conditions in ADHD

Oppositional defiant disorder and conduct disorder

The defiant and aggressive behaviour that defines oppositional defiant disorder and the more severe conduct disorder, is highly comorbid with ADHD,⁴² and distinguishing between the two disorders can be difficult as the impulsivity that comes with ADHD often makes children act aggressively. Careful teasing out of the core symptoms of ADHD will enable differentiation

Autism spectrum disorder

Estimations vary substantially but prevalence rates of 20-50% have been reported for children with ADHD also meeting criteria for autism spectrum disorder.⁴³ It is therefore essential to include screening questions such as how able is the child to appreciate another person's perspective

Tic disorders

Compared with controls, children with ADHD are at an increased risk of developing tic disorders42

Poor motor coordination

ADHD is often accompanied by delays in motor milestones, difficulties with writing, clumsiness, and poor performance in sports⁴⁴

Specific learning difficulties

Dyslexia is commonly associated with ADHD. Reading comprehension is reduced in children with ADHD; linked to deficits in working memory⁴⁵

Sleep disorders

Sleep disorders are commonly associated with ADHD and often overlooked.⁴⁶ It is important to determine whether there is a primary sleep disorder leading to problems with attention and concentration or whether the child has trouble settling to sleep because of ADHD. In the history it is also important to rule out obstructive sleep apnoea

Emotional disorders

Anxiety and depression are often concomitant with ADHD.⁴² These symptoms may be related to ADHD or problems in interpersonal relationships

Early adversity

Prolonged disruption of relationships in early childhood can lead to attachment disorders. These may present as indiscriminate behaviours towards adults and peers and inattentive behaviours that resemble ADHD.⁴⁷ However, having an attachment disorder does not rule out ADHD. Children who have experienced extreme institutional deprivation, as in the case of the Romanian orphans, have both significantly increased levels of inattention and overactivity and disinhibited attachment.⁴⁸ It is unclear whether less extreme forms of deprivation are associated with ADHD⁴⁹

Bipolar disorder

Controversial studies indicate a large overlap between bipolar disorder in children and ADHD,⁵⁰⁵¹ with no consensus on treatment implications

Substance use disorder

ADHD is present in almost a quarter of adults with substance use disorder,⁵² with patterns of misuse often starting in adolescence

Fetal alcohol syndrome

ADHD symptoms are seen in children with fetal alcohol syndrome and the hyperactivity symptoms often respond to ADHD drugs⁵³

knowledge but in acting on a thought or idea before thinking about the consequences of this behaviour.⁶⁴

Cognitive training and cognitive behavioural therapy

Cognitive training involves the training of attention and working memory, which are often considered part of "executive function." A systematic review and meta-analysis of randomised controlled trials of cognitive training for ADHD symptoms found no evidence of efficacy when using "probably" blinded assessors.55 Cognitive training was found to be effective when non-blinded assessors were used. For cognitive behavioural therapy (CBT), a review of the literature in 2010 found no studies indicating that CBT was helpful for ADHD symptoms in children.⁵⁸ However, evidence from a subsequent non-randomised controlled trial indicates that CBT may be helpful for adolescents with ADHD who are receiving drugs and have residual difficulties.⁶⁵ The effects were better for adolescents with comorbid anxiety and depression compared with those with comorbid conduct disorder or oppositional defiant disorder.

Classroom interventions

In traditional educational settings, children with ADHD can struggle to control their behaviour, achieve academically, and manage peer relationships.⁶⁴ There is some evidence for the positive effects of school based intervention, although contextual factors and the perceptions of students and staff play an important role.⁶⁶ Advice for teachers has been shown to be useful in managing children with ADHD, delivered, for example, in leaflets, with significant positive effects on attitudes and

For personal use only: See rights and reprints http://www.bmj.com/permissions

a with ADHD can e academically, and e evidence for the although contextual staff play an n shown to be useful

117

behaviour but not on attainment.⁶⁷ Examples of effective classroom strategies include giving pupils a choice of two or more concurrently presented classroom activities,⁶⁷ sitting pupils near teachers so that they can be prompted if attention wanders, breaking down tasks and instructions,⁶⁴ and using immediate rewards (stickers or points) for wanted behaviour and mild penalties when "off task."⁶⁸ Teachers find using daily report cards, which enhance teacher-parent collaboration, a useful intervention.⁶⁶ A further study has shown how certain types of movement, for example sitting on an activity ball, can actually assist in focusing a child's attention, contrary to concerns that such activity might exacerbate inattention.⁶⁹ There have been some positive academic effects with a class peer tutoring system.⁷⁰ There is no evidence that classroom social skills training helps peer interactions for those with ADHD,⁵⁶ but peer mediated resolution of conflicts has been associated with school-wide reductions in playground violence and negative interactions.⁷¹ Class-wide interventions—for example, to reduce distraction—are probably the least stigmatising to implement.⁶⁶

Dietary advice

The importance of a healthy, balanced diet and regular exercise needs to be emphasised for all children, including those with ADHD. If there is a history suggesting the negative influence of certain foods then a food diary can help to determine these links. In the UK, NICE recommends that when certain foods are linked with difficult behaviour then specific elimination diets should be jointly managed by a dietician and the treating specialist.³⁶ A randomised controlled trial using non-blinded assessors (parents) suggests that a "restricted elimination diet," whereby the diet was reduced to a few basic foods and then

Page 6 of 14

gradually broadened to assess other foods, found a dramatic reduction in ADHD symptoms in children not receiving drugs.72 However, a subsequent systematic review and meta-analysis of randomised controlled trials using blinded assessors found insufficient evidence for the efficacy of restricted elimination diets,⁵⁵ although the exclusion of artificial food colourants had a moderate positive effect on ADHD symptoms. The authors commented that children in both the restricted elimination diet and the artificial food colour exclusion trials were often preselected on the basis of sensitivity to certain food types, so the positive results may be applicable only to children with suspected food sensitivities.55 The use of free fatty acid supplementation can benefit some children with ADHD, as supported by the same meta-analysis of randomised controlled trials, with an effect size around 0.3, which is significant but small compared with drugs, which can have effect sizes of 0.7-1.0.55 We have summarised the evidence for non-drug treatment for ADHD in table $1 \downarrow$.

Drugs

Drugs can improve the three core symptoms of inattention, overactivity, and impulsivity,³⁶ and there is evidence from randomised controlled trials to support the use of drugs for symptomatic and functional improvement in the short term. As described above, children without ADHD treated with drugs also show improvements in attention and focus,^{27 28} leading to drugs being considered performance enhancing rather than as specific treatment for the psychopathology of ADHD.³⁴

There are two main groups of clinically effective drugs for ADHD: psychostimulants, which increase available central dopamine and noradrenaline (for example, methylphenidate and dexamfetamine), and others, which include noradrenergic reuptake inhibitors (for example, atomoxetine). The choice of drug depends on the needs of the young person, formulation of the drug, ratio of immediate to extended release components, side effect profile, and cost (table $2\Downarrow$).

A systematic review of randomised controlled trials provides evidence that psychostimulants and atomoxetine improve the core symptoms of ADHD and improve quality of life, although limitations of the studies for dexamphetamine and methylphenidate were noted.⁷³ Short and long acting formulations of methylphenidate have been found to be equally effective.⁷⁴ The overall effect size for methylphenidate is estimated at 1.0^{75} and for atomoxetine at 0.7,⁷⁶ with other studies reporting a number needed to treat of 3 for methylphenidate (extended release) and 5 for atomoxetine.⁷⁴ A few studies have explored the experiences of children with ADHD receiving drugs-for example, one small study reported generally positive experiences of treatment.³⁶ The children described putting up with the "annoying" aspects of drugs in return for improved relationships with peers as a result of less disruptive behaviour. The more common adverse effects of drugs for ADHD are nausea, headaches, sleep problems, slight increases in heart rate and blood pressure, and decreased appetite with associated weight loss and reduction in height; more details are provided in box 3.77

Although there is evidence that current and active psychostimulant treatment (of any duration) is associated with symptomatic and functional improvement, longer term follow-up studies were not able to show beneficial effects of stimulant use on ADHD symptoms and overall functioning in the longer term.⁷⁸ None of the studies accounted for the variable course of the disorder over childhood, drug adherence, and selection bias in treatment.³⁵

In light of the evidence on the effectiveness of drugs for ADHD, the choice to start treatment should primarily be considered in severe cases where impairment is demonstrable in multiple areas of the child's life. An honest discussion with parents and older children about the benefits and uncertainties of treatment and possible adverse effects is recommended.

Initiation, titration, and monitoring of drug treatment

When drug treatment for ADHD is initiated and monitored in secondary care by child psychiatrists or paediatricians, primary care professionals have an important role in alerting overseeing specialists to problems in the overall treatment plan, such as non-compliance, or in expediting a review of the current treatment plan if difficulties arise. NICE recommends (based on effectiveness, side effect profile, and cost) methylphenidate as first line treatment for severe ADHD, followed by atomoxetine and then dexamphetamine.³⁶

Initiation—Treatment regimens usually start with immediate release methylphenidate.³⁶ Once-daily doses, although more costly, may be more practical and less stigmatising, and as psychostimulants are controlled drugs some schools do not want to administer them. Different preparations of immediate release and extended release are available (table 2) enabling flexibility if, for example, only the school day needs to be targeted or additional evening doses are required.

Titration—Response to treatment is initially monitored and titrated closely to determine the optimal dose, which should ideally be reached within a few weeks.³⁶

Monitoring—Careful and systematic follow-up of children taking psychotropic drugs is of utmost importance. There should be clinical follow-up to monitor the psychological and behavioural effects of drugs after each change in dose, then at three months and routinely every six months, when height, weight, heart rate, and blood pressure should also be recorded (see box 3). These reviews should also include information from teachers to establish how well the symptoms are being controlled at school. Rating scales can be used to monitor clinical and behavioural change (see table on thebmj.com for examples of ADHD rating scales).⁷⁹

Duration of treatment and managing comorbidities

After an adequate treatment response, drug treatment should be continued for as long as it remains effective, with at least biannual review. Drug holidays are not routinely recommended. The decision as and when to stop drugs is one that must be informed by what the children and parents want along with clinically perceived efficacy of treatment. If children no longer want to take drugs or the parents think they would like their child to try a period without drugs, then it is important to support this request. Drugs should ideally not be stopped at times of transition or increased stress (for example, when moving schools or sitting examinations), and summer holidays can be an opportune time for dose reduction. Table 3U provides more information on how to manage different drugs.

Often specialist advice is needed in the drug treatment of psychiatric comorbidities. Selective serotonin reuptake inhibitors for depression and some anxiety disorders are tolerated with methylphenidate. For sleep disorders, sleep hygiene should be considered a first line treatment, and specialist drug intervention, such as melatonin, may be useful, but only under specialist care.

CLINICAL REVIEW

Box 3 Managing the adverse effects of drug treatment

Neurological

Headaches, irritability, and dizziness

Disappear spontaneously or on dose reduction³⁶

Insomnia

Evidence is inconsistent and clinical experience suggests that there is considerable individual variability in how children's sleep is affected: some experience no effect while others can settle more easily a few hours after taking psychostimulants and some are unable to sleep because of the stimulating effects of the drugs and so will need to either change the drug or ensure shorter acting preparations are taken^{77 80}

Tics

Not a contraindication to drug treatment, tics can sometimes be worsened by psychostimulant drugs and can be improved by atomoxetine.⁷⁷ Observe over three months, as the natural, fluctuating course of tics can lead them to be more and less prominent over time, independent of drugs

Epilepsy

ADHD drugs lower the seizure threshold but can be used in children with established epilepsy with specialist monitoring⁷⁷

Cardiovascular

Blood pressure

All ADHD drugs have the potential to increase blood pressure and pulse and so both must be routinely monitored. In most cases the changes are small (average increases of 1-4 mm Hg for systolic and 1-2 mm Hg for diastolic pressure and 1-2 beats/min for pulse), however in a subset of children (5-15%) the increases in blood pressure and pulse may be above the 95th centile (measured three times within one visit with an age adjusted cuff) and children should be referred to specialist care⁶¹

Severe cardiovascular events

Children with a congenital heart defect, a history of cardiac symptoms (for example, syncope on exercise), or a positive family history of sudden death below the age of 40 years, are at risk of sudden death.⁷⁷ For these children extra caution needs to be taken with ADHD drugs and the involvement of a paediatric cardiologist is needed

Gastrointestinal

Nausea

Can disappear spontaneously or on dose reduction

Weight loss and reduced appetite

Psychostimulants reduce appetite with weight loss usually most pronounced in the first six months of treatment.⁸² Drugs are therefore best taken with or after food (advise additional snacks early in the morning or late in the evening)

Liver damage

May be a rare, idiosyncratic, and mostly reversible effect of atomoxetine.⁸³ Routine blood screening and monitoring are not recommended but advise seeking urgent medical opinion if abdominal pain, nausea, dark urine, or jaundice emerge³⁶

Growth

Reduced height

Variable effect of psychostimulants on growth, with a delay of approximately 1 cm/year in the first three years. The effect may be dose dependent and reversible when treatment is stopped. It is unclear whether stimulants have an effect on final adult height. Atomoxetine has similar effects on growth to stimulants.⁸⁴ If height measurements drop on the centile charts then a dose reduction is recommended, as can be switching to an alternative formulation or including some drug holidays in the treatment regimen. If height is significantly affected then referral to an endocrinologist is warranted⁷⁷

Psychological symptoms

Psychotic symptoms

Very rarely delusions, hallucinations, and mania can emerge during treatment⁷⁷

Suicidal thoughts

There is a reported slight increase in suicidal thoughts when starting atomoxetine; therefore mood must be monitored on initiation of treatment. Suicidal thoughts are not a contraindication to treatment, but dose reduction might be warranted⁷⁷

Other

Drug misuse

There is no evidence that treatment with psychostimulants increases the risk for later drug misuse.⁸⁵ A subsample of children with ADHD may be prone to misuse of psychostimulants. Dexamphetamine has the highest potential for misuse, and, in high risk cases, modified release methylphenidate, lisdexamfetamine, or atomoxetine should be considered⁷⁷

Sexual dysfunction

Erectile and ejaculatory dysfunction and dysmenorrhoea are potential side effects of atomoxetine

We thank David Coghill, Tamsin Ford, Brian Green, Sandra Hallett, Ilja Holland-Kaye, Alison Maycock, Neysan Pucks, and Ruth Reed for helpful comments on earlier drafts of the review; the reviewers for their thoughtful and comprehensive comments; the BMJ editors who provided considerable input to the review, and all who in combination contributed to a much improved publication. We are grateful for permission from Professor Asherson and UKAAN for allowing us to revise a slide on ADHD impact. We thank the young adult and parent who kindly shared their experience with us. Contributors: NV analysed the data. MF and NV wrote the first draft of the review. NV, MF, and MP revised drafts of the paper. MF is the guarantor.

Competing interests: We have read and understood the BMJ policy on declaration of interests and declare the following: none.

Provenance and peer review: Not commissioned; externally peer reviewed.

CLINICAL REVIEW

A young person's story

I wasn't diagnosed until I was 11 when my family moved and I had to repeat a school year. I had performed well in a well-structured parochial school but started to slide when put in a more loosely structured school. I was prescribed medication for ADHD and given counselling on how to best organise and manage my time.

I never liked to be medicated (methylphenidate); the drugs gave me a dull and disconnected sense where I felt a physical distance between others and myself. My resistance to taking medication caused an ongoing fight between my mother and me. She wanted the best for me and bought me a fancy watch with five separate alarms to help me remember to take my meds.

In secondary school I learned to manage my ADHD: I used natural stimulants like coffee, began to meditate, and participated in attention intensive sports like rowing. These practices, along with the strategies I had learned to organise my time, helped me cope. At university I abandoned medication altogether when I was tempted to use it as a diet aid. Now, 17 years since diagnosis, I don't take medicine at all, though I think it would have been helpful at times during graduate school. I've found that things that fall inside my organisational structures get done quite well, and I'm surprised when employers laud my organisational skills, which are strong enough to organise whole teams and offices.

My family has not adapted to my increased capacities, and I find that interesting and sometimes very challenging. That said, if it's not on the list, it's likely not going to get done any time soon. And if I'm in between the notebooks I keep my list in, little's going to be accomplished.

A parent's story

In our son's last few years of school we realised that normal school challenges had become major challenges for him. Although he had managed an extremely busy school schedule, as school pressures increased we noticed that he had to work into the night to keep up with his studies. His normal fidgetiness and procrastination had become completely unmanageable. He would start new tasks before finishing others. His thoughts were scattered. He could not maintain focus for more than 10 minutes without getting up to snack or take a break. After six hours on an assignment he would have completed only 2-3 sentences.

For the first time our son lost his self esteem. He started to remark that he wasn't as smart as his classmates. I remember him telling me that sometimes he had to just stare at a blank white wall for 15 minutes to clear his mind.

Following medical review he was prescribed Concerta. Overnight his thoughts became more focused, he started to work methodically through his assignments, and normal sleep patterns came back. Most importantly, our son regained his sense of self esteem.

At university our son never lost the feeling that he should try and conquer ADHD without the benefit of medication. He began to realise that his ADHD symptoms were much more pronounced when he was forced to fulfill an academic requirement not in his core competencies. A physician counselled him to use Concerta selectively, to get through the more arduous tasks. She also helped him re-frame his perception of the condition not as a disability but as a special trait, which bestowed significant benefits on the aesthetic career path he had chosen.

Questions for future research

- What is the optimal duration for drug treatments and what are their long term effects?
- · What are the best classroom strategies for managing ADHD, and how can they be implemented to support children and staff?
- · Is parent training best delivered individually or in groups and is it more effective for certain clusters of symptoms?
- · Can treatments be tailored for specific subgroups with ADHD?
- Does screening for ADHD and associated comorbidities play a role for school children at risk of exclusion or poor academic attainment?
- · Is there a role for games, apps, and digital media in the management of ADHD?
- · What are the long term outcomes of ADHD when children become adults, and which are the best treatment options for adults?
- Ford T, Goodman R, Meltzer H. The British Child and Adolescent Mental Health Survey 1999: the prevalence of DSM-IV disorders. J Am Acad Child Adolesc Psychiatry 2003;42:1203-11.
- 2 Erskine HE, Ferrari AJ, Nelson P, et al. Epidemiological modelling of attention-deficit/hyperactivity disorder and conduct disorder for the Global Burden of Disease Study 2010. J Child Psychol Psychiatry 2013;54:1263-74.
- 3 Gardner DM, Gerdes AC. A review of peer relationships and friendships in youth with ADHD. J Atten Disord 2013; published online 23 Sep.
- 4 Pimentel MJ, Vieira-Santos S, Santos V, et al. Mothers of children with attention deficit/hyperactivity disorder: relationship among parenting stress, parental practices and
- child behaviour. *Atten Defic Hyperact Disord* 2011;3:61-8. 5 Babinski LM, Hartsough CS, Lambert NM. Childhood conduct problems,
- hyperactivity-impulsivity, and inattention as predictors of adult criminal activity. J Child Psychol Psychiatry 1999;40:347-55.
- 6 Parker C, Whear R, Ukoumunne OC, et al. School exclusion in children with psychiatric disorder or impairing psychopathology: a systematic review. *Emot Behav Difficult* 2014; published online 20 Aug. doi:10.1080/13632752.2014.945741.
- 7 Molina BS, Hinshaw SP, Swanson JM, et al. The MTA at 8 years: prospective follow-up of children treated for combined-type ADHD in a multisite study. J Am Acad Child Adolesc Psychiatry 2009;48:484-500.
- 8 Sayal F, Washbrook E, Propper C. Childhood behavior problems and academic outcomes in adolescence: longitudinal population-based study. J Am Acad Child Adolesc Psychiatry 2015;54:360-8.
- 9 Angold A, Erkanli A, Egger HL, et al. Stimulant treatment for children: a community perspective. J Am Acad Child Adolesc Psychiatry 2000;39:975-84.
- 10 Thapar A, Cooper M, Eyre O, et al. Practitioner review: what have we learnt about the causes of ADHD? J Child Psychol Psychiatry 2013;54:3-16.
- 11 Faraone SV, Perlis RH, Doyle AE, et al. Molecular genetics of attention-deficit/ hyperactivity disorder. Biol Psychiatry 2005;57:1313-23.
- 12 Cross-Disorder Group of the Psychiatric Genomics Consortium. Identification of risk loci with shared effects on five major psychiatric disorders: a genome-wide analysis. *Lancet* 2013;381:1371-9.
- 13 Shah PJ, Morton MJ. Adults with attention-deficit hyperactivity disorder—diagnosis or normality? Br J Psychiatry 2013;203:317-9.
- Parens E, Johnston J. Facts, values, and attention-deficit hyperactivity disorder (ADHD): an update on the controversies. *Child Adolesc Psychiatry Ment Health* 2009;3:1.
 Batter L. Nieuwa E. H. Ledders, *March Exploring fue agroups accurate an attention*.
 - 15 Batstra L, Nieweg EH, Hadders-Algra M. Exploring five common assumptions on attention deficit hyperactivity disorder. Acta Paedatr 2014;103:696-700.

- 16 Schwarz A, Cohen S. A.D.H.D. seen in 11% of U.S. children as diagnoses rise. New York Times 2013 Mar 31.
- 17 Asherson P, Trzaskowski M. Attention-deficit/hyperactivity disorder is the extreme and impairing tail of a continuum. J Am Acad Child Adolesc Psychiatry 2015;54:249-50.
- 18 Levy F, Hay DA, McStephen M, et al. Attention-deficit hyperactivity disorder: a category or a continuum? Genetic analysis of a large-scale twin study. J Am Acad Child Adolesc Psychiatry 1997;36:737-44.
- 19 Stergiakouli E, Martin J, Hamshere ML, et al. Shared genetic influences between Attention-Deficit/ Hyperactivity Disorder (ADHD) traits in children and clinical ADHD. J Am Acad Child Adolesc Psychiatry 2015;54:322-7.
- 20 Larsson H, Anckarsater H, Råstam M, et al. Childhood attention-deficit hyperactivity disorder as an extreme of a continuous trait: a quantitative genetic study of 8,500 twin pairs. J Child Psychol Psychiatry 2012;53:73-80.
- 21 Frances A. The past, present and future of psychiatric diagnosis. World Psychiatry 2013;12:111-2.
- 22 Monynihan R. A new deal on disease definition. BMJ 2011;342:1136.
- 23 Visser SN, Danielson ML, Bitsko RH, et al. Trends in the parent-report of health care provider-diagnosed and medicated attention-deficit/hyperactivity disorder: United States, 2003-2011. J Am Acad Child Adolesc Psychiatry 2014;53:34-46.
- 24 Russell G, Rodgers LR, Ukoumunne OC, et al. Prevalence of parent-reported ASD and ADHD in the UK: findings from the Millennium Cohort Study. J Autism Dev Disord 2014:44:31-40.
- 25 McCarthy S, Wilton L, Murray ML, et al. The epidemiology of pharmacologically treated attention deficit hyperactivity disorder (ADHD) in children, adolescents and adults in UK primary care. *BMC Pediatr* 2012;12:78.
- 26 Singh I, Filipe AM, Bard I, et al. Globalization and cognitive enhancement: emerging social and ethical challenges for ADHD clinicians. *Curr Psychiatry Rep* 2013;15:385.
- 27 Rapoport JL, Buchsbaum MS, Weingartner H, et al. Dextroamphetamine. Its cognitive and behavioral effects in normal and hyperactive boys and normal men. Arch Gen Psychiatry 1980;37:933-43.
- 28 Del Campo N, Fryer TD, Hong YTA, et al. Positron emission tomography study of nigro-striatal dopaminergic mechanisms underlying attention: implications for ADHD and its treatment. *Brain* 2013;136:3252-70.
- 29 Swanson JM, Sergeant JA, Taylor E, et al. Attention-deficit hyperactivity disorder and hyperkinetic disorder. *Lancet* 1998;351:429-33.
- 30 First MB. Harmonisation of ICD-11 and DSM-V: opportunities and challenges. Br J Psychiatry 2009;195:382-90.

Page 9 of 14

CLINICAL REVIEW

Additional educational resources

Resources for healthcare professionals

National Institute for Health and Care Excellence guideline. Attention deficit hyperactivity disorder: diagnosis and management of ADHD in children, young people and adults (www.nice.org.uk/CG72)—evidence based guidelines on ADHD management in the UK

Cortese S, Holtmann M, Banaschewski T, et al. Current best practice in management of adverse events during treatment with ADHD medication in children and adolescents. *J Child Psychol Psychiatry* 2013;54:227-46. http://onlinelibrary.wiley.com/doi/10.1111/jcpp. 12036/epdf—guidelines on management of adverse effects of medication produced on behalf of the European ADHD Guidelines Group

The NIMH-funded Multimodal Treatment of Attention Deficit Hyperactivity Disorder (MTA) study (www.nimh.nih.gov/funding/clinicaltrials-for-researchers/practical/mta/multimodal-treatment-of-attention-deficit-hyperactivity-disorder-mta-study.shtml)—a multisite study designed to evaluate the main interventions for ADHD, including behavior therapy, drugs, and the combination of the two. First study published in 1999 and follow-up continues

Resources for young people and their families

The National Attention Deficit Disorder Information and Support Service UK. ADDISS (www.addiss.co.uk/)—a patient and parent support organization

Young minds (www.youngminds.org.uk/for_children_young_people/whats_worrying_you/adhd)—information on ADHD tailored for young people

American Academy of Child and Adolescent Psychiatry and American Psychiatric Association (www.parentsmedguide.org/pmg_adhd. html)—ADHD drug information for parents

NHS choices. Attention Deficit Hyperactivity Disorder (ADHD) (www.nhs.uk/conditions/Attention-deficit-hyperactivity-disorder/Pages/ Introduction.aspx)—includes a video clip of an interview between a psychiatrist and a child with ADHD and his parents

Green C, Chee K. Understanding ADHD. A parent's guide to attention deficit hyperactivity disorder in children. Vermilion, 1997–a book with useful information and helpful strategies for parents and teachers

Hoopman K. All dogs have ADHD. Jessica Kingsley, 2008-a useful, light hearted book illustrating some aspects of ADHD

www.healthline.com/health-slideshow/top-adhd-android-iphone-apps—a review of some of the ADHD apps available in 2015. Healthline (www.healthline.com/health/adhd)—has information and links to a range of blogs on ADHD and selected videos on YouTube and Tedx for young people and their families

ADHDVoices. YouTube. What's it like to have ADHD? (www.youtube.com/watch?v=HI7Ro1PUJmE)—short animated video of what it is like to have ADHD from a young person's perspective

- 31 Moncrieff J, Timimi S. The social and cultural construction of psychiatric knowledge: an
- analysis of NICE guidelines on depression and ADHD. Anthropol Med 2013;20:59-71.
 Mitchell J, Read J. Attention-deficit hyperactivity disorder, drug companies and the internet. Clin Child Psychol Psychiatry 2012;17:121-39.
- 33 INCB. Report of the International Narcotics Control Board 2013. New York: United Nations, 2014.
- Singh I. Beyond polemics: science and ethics of ADHD. *Nat Rev Neurosci* 2008;9:957-64.
 Hazell P. The challenges to demonstrating long-term effects of psychostimulant treatment
- for attention-deficit/hyperactivity disorder. Curr Opin Psychiatry 2011;24:286-90.
 National Institute for Health and Care Excellence. Attention deficit hyperactivity disorder: diagnosis and management of ADHD in children, young people and adults. (Clinical
- guideline C72.) 2008, modified 2013. www.nice.org.uk/guidance/CG72.
 American Academy of Pediatrics. ADHD: clinical practice guideline for the diagnosis, evaluation, and treatment of attention-deficit/hyperactivity disorder in children and adolescents. *Pediatrics* 2011;128:1007-22.
- 38 Klasen H, Goodman R. Parents and GPs at cross-purposes over hyperactivity: a qualitative study of possible barriers to treatment. Br J Gen Pract 2000;50:199-202.
- 39 Singh I. Doing their jobs: mothering with Ritalin in a culture of mother-blame. Soc Sci Med 2004;59:1193-205.
- Sayal K, Taylor E, Beecham J, et al. Pathways to care in children at risk of attention-deficit hyperactivity disorder. *Br J Psychiatry* 2002;181:43-8.
 Sayal K, Goodman R, Ford T. Barriers to the identification of children with attention
- 41 Sayal K, Goodman R, Ford T. Barriers to the identification of children with attention deficit/hyperactivity disorder. *J Child Psychol Psychiatry* 2006;47:744-50.
- 42 Yoshimasu K, Barbaresi WJ, Colligan RC, et al. Childhood ADHD is strongly associated with a broad range of psychiatric disorders during adolescence: a population-based birth cohort study. J Child Psychol Psychiatry 2012;53:1036-43.
- 43 Rommelse NN, Franke B, Geurts HM, et al. Shared heritability of attention-deficit/hyperactivity disorder and autism spectrum disorder. *Eur Child Adolesc Psychiatry* 2010;19:281-95.
- 44 Fliers E, Vermeulen S, Rijsdijk F, et al. ADHD and poor motor performance from a family genetic perspective. J Am Acad Child Adolesc Psychiatry 2009;48:25-34.
- 45 Miller AC, Keenan JM, Betjemann RS, et al. Reading comprehension in children with ADHD: cognitive underpinnings of the centrality deficit. J Abnorm Child Psychol 2013;41:473-83.
- 46 Sung V, Hiscock H, Sciberras E, et al. Sleep problems in children with attention-deficit/hyperactivity disorder: prevalence and the effect on the child and family. *Arch Pediatr Adolesc Med* 2008;162:336-42.
- 47 Taylor E, Dopfner M, Sergeant J, et al. European clinical guidelines for hyperkinetic disorder—first upgrade. Eur Child Adolesc Psychiatry 2004;13(Suppl 1):17-30.
- 48 Rutter M, Beckett C, Castle J, et al. Effects of profound early institutional deprivation: an overview of findings from a UK longitudinal study of Romanian adoptees. *Eur J Dev Psychol* 2007;4:332-50.
- 49 Kreppner JM, Rutter M, Beckett C, et al. Normality and impairment following profound early institutional deprivation: a longitudinal follow-up into early adolescence. *Dev Psychol* 2007;43:931-46.
- 50 Biederman J, Faraone S, Mick E, et al. Attention-deficit hyperactivity disorder and juvenile mania: an overlooked comorbidity? J Am Acad Child Adolesc Psychiatry 1996;35:997-1008.
- Hassan A, Agha SS, Langley K, et al. Prevalence of bipolar disorder in children and adolescents with attention-deficit hyperactivity disorder. *Br J Psychiatry* 2011;198:195-8.
 Van Emmerik-van Oortmerssen K, van de Glind G, van den Brink W, et al. Prevalence
- of attention-deficit hyperactivity disorder in substance use disorder patients: a meta-analysis and meta-regression analysis. *Drug Alcohol Depend* 2012;122:11-9.
 Peadon E, Rhvs-Jones B, Bower C, et al. Systematic review of interventions for children
- 121 38 Peadon E, Rhys-Jones B, Bower C, et al. Systematic review of interventions for children with fetal alcohol spectrum disorders. *BMC Pediatr* 2009;9:35.

- 54 Shaffer D, Gould MS, Brasic J, et al. A Children's Global Assessment Scale (CGAS). Arch Gen Psychiatry 1983;40:1228-31.
- 55 Sonuga-Barke EJ, Brandeis D, Cortese S, et al. Nonpharmacological interventions for ADHD: systematic review and meta-analyses of randomized controlled trials of dietary and psychological treatments. *Am J Psychiatry* 2013;170:275-89.
- 56 Storebo OJ, Skoog M, Damm D, et al. Social skills training for Attention Deficit Hyperactivity Disorder (ADHD) in children aged 5 to 18 years. *Cochrane Database Syst Rev* 2011;12:CD008223.
- 57 Zwi M, Jones H, Thorgaard C, et al. Parent training interventions for Attention Deficit Hyperactivity Disorder (ADHD) in children aged 5 to 18 years. *Cochrane Database Syst Rev* 2011;12:CD003018.
- 58 Young S, Amarasinghe M. Practitioner review: non-pharmacological treatments for ADHD: a lifespan approach. J Child Psychol Psychiatry 2010;51:116-33.
- 59 MTA Cooperative Group. A 14-month randomized clinical trial of treatment strategies for attention-deficit/hyperactivity disorder. Arch Gen Psychiatry 1999;56:1073-86.
- 60 MTA Cooperative Group. National Institute of Mental Health Multimodal Treatment Study of ADHD follow-up: 24-month outcomes of treatment strategies for attention-deficit/hyperactivity disorder. *Pediatrics* 2004;113:754-61.
- 61 Sonuga-Barke EJ, Daley D, Laver-Bradbury C, et al. Parent-based therapies for preschool Attention-Deficit/Hyperactivity Disorder: a randomized, controlled trial with a community sample. J Am Acad Child Adolesc Psychiatry 2001;40:402-8.
- 62 Webster-Stratton C, Hancock L. Parent training for young children with conduct problems: content, methods and therapeutic process. In: Briesmeister JM, Schaefer CE, eds. Handbook of parent training: parents as co-therapists for children's behaviour problems. 2nd ed. Wiley. 1998.
- 63 National Institute of Health and Care Excellence. Antisocial behaviour and conduct disorders in children and young people: recognition, intervention and management. (Clinical guideline CG158.) 2013. www.nice.org.uk/guidance/cg158.
- 64 DuPaul GJ, Weyandt LL. School-based intervention for children with attention deficit hyperactivity disorder: effects on academic, social, and behavioural functioning. Int J Dis Dev Educ 2006;53:161-76.
- 65 Antshel KM, Faraone SV, Gordon M. Cognitive behavioural treatment outcomes in adolescent ADHD. J Atten Disord 2012;18:483-95.
- 66 Moore D, Richardson M, Gwernan-Jones R, et al. Non-pharmacological interventions for ADHD in school settings: an overarching synthesis of systematic reviews. J Attention Dis 2015; published online 9 Mar.
- 67 Dunlap G, dePerczel M, Clarke S, et al. Choice making to promote adaptive behavior for students with emotional and behavioral challenges. J Applied Behav Anal 1994;27:505-18.
- 68 DuPaul GJ, Guevremont DC, Barkley RA. Behavioral treatment of attention-deficit hyperactivity disorder in the classroom. The use of the attention training system. *Behav Modif* 1992;16:204-25.
- 69 Sarver DE, Rapport M, Kofler MJ, et al. Hyperactivity in Attention-Deficit/Hyperactivity Disorder (ADHD): impairing deficit or compensatory behavior? J Abnorm Child Psychol 2015; published online 12 Apr.
- 70 DuPaul GJ, Ervin RA, Hook CL, et al. Peer tutoring for children with attention deficit hyperactivity disorder: effects on classroom behaviour and academic performance. J Appl Behav Anal 1998;31:579-92.
- 71 Cunningham CE, Cunningham LJ, Martorelli V, et al. The effects of primary division, student-mediated conflict resolution programs on playground aggression. J Child Psychol Psychiatry 1998;39:653-62.
- 72 Pelsser LM, Frankena K, Toorman J, et al. Effects of a restricted elimination diet on the behaviour of children with attention-deficit hyperactivity disorder (INCA study): a randomised controlled trial. *Lancet* 2011;377:494-503.
- 73 King S, Griffin S, Hodges Z, et al. A systematic review and economic model of the effectiveness and cost-effectiveness of methylphenidate, dexamfetamine and atomoxetine

for the treatment of attention deficit hyperactivity disorder in children and adolescents. *Health Technol Assess* 2006;10:iii-iv, xiii-146. Banaschewski T, Coghill D, Santosh P, et al. Long-acting medications for the hyperkinetic

- 74 Banaschewski T, Coghill D, Santosh P, et al. Long-acting medications for the hyperkinetic disorders. A systematic review and European treatment guideline. *Eur Child Adolesc Psychiatry* 2006;15:476-95.
- 75 Pliszka S, AACAP Work Group on Quality Issues. Practice parameter for the assessment and treatment of children and adolescents with attention-deficit/hyperactivity disorder. J Am Acad Child Adolesc Psychiatry 2007;46:894-921.
- 76 Michelson D, Allen AJ, Busner J, et al. Once-daily atomoxetine treatment for children and adolescents with attention deficit hyperactivity disorder: a randomized, placebo-controlled study. Am J Psychiatry 2002;159:1896-901.
- 77 Cortese S, Holtmann M, Banaschewski T, et al. Practitioner review: current best practice in the management of adverse events during treatment with ADHD medications in children and adolescents. J Child Psychol Psychiatry 2013;54:227-46.
- 78 Riddle MA, Yershova K, Lazzaretto D, et al. The Preschool Attention-Deficit/Hyperactivity Disorder Treatment Study (PATS) 6-year follow-up. J Am Acad Child Adolesc Psychiatry 2013;52:264-78.e2.
- 79 Collett BR, Ohan JL, Myers KM. Ten-year review of rating scales. V: scales assessing attention-deficit/hyperactivity disorder. J Am Acad Child Adolesc Psychiatry 2003;42:1015-37.
- 80 Cortese S, Faraone SV, Konofal E, et al. Sleep in children with attention-deficit/hyperactivity disorder: meta-analysis of subjective and objective studies. J Am Acad Child Adolesc Psychiatry 2009;48:894-908.

- 81 Hammerness PG, Perrin JM, Shelley-Abrahamson R, et al. Cardiovascular risk of stimulant treatment in pediatric attention-deficit/hyperactivity disorder: update and clinical recommendations. J Am Acad Child Adolesc Psychiatry 2011;50:978-90.
- 82 Poulton A, Briody J, McCorquodale T, et al. Weight loss on stimulant medication: how does it affect body composition and bone metabolism? A prospective longitudinal study. Int J Pediatr Endocrinol 2012;2012:30.
- Bangs ME, Jin L, Zhang S, et al. Hepatic events associated with atomoxetine treatment for attention-deficit hyperactivity disorder. *Drug Saf* 2008;31:345-54.
 Kratochvil CJ, Wilens TE, Greenhill LL, et al. Effects of long-term atomoxetine treatment
- 84 Kratochvil CJ, Wilens TE, Greenhill LL, et al. Effects of long-term atomoxetine treatment for young children with attention-deficit/hyperactivity disorder. J Am Acad Child Adolesc Psychiatry 2006;45:919-27.
- 85 Chang Z, Lichtenstein P, Halldner L, et al. Stimulant ADHD medication and risk for substance abuse. J Child Psychol Psychiatry 2014;55:878-85.
- Yemula C, Besag F, Coghill D. How is standard ADHD medication used in clinical practise and how is this supported by research? *Cut Edge Psychiatry Pract* 2013;2:35-45.
 American Psychiatric Association. Diagnostic and statistical manual of mental disorders.
- American Psychiatric Association. Diagnostic and statistical manual of mental disorders.
 5th ed. APA, 2013.

Cite this as: BMJ 2015;350:h2168

© BMJ Publishing Group Ltd 2015

Tables

Table 1| Evidence for non-drug treatment for attention-deficit/hyperactivity disorder (ADHD)

Treatment	Level of evidence	Evidence
Parent training	1*	Insufficient evidence ⁵⁵
Cognitive training	1	More evidence needed ⁵⁵
Cognitive behavioural therapy	3†	Shown to be effective in adolescents receiving ADHD drug treatments ⁶⁵
Social skills training	1	Insufficient evidence ⁵⁶
Free fatty acid supplementation	1	Small but significant effects; clinical significance to be determined ⁵⁵
Artificial food colour exclusion	1	Statistically significant, modest effects on ADHD symptoms ⁵⁵
Restricted elimination diets	1	Insufficient evidence ⁵⁵

Levels of evidence from Oxford Centre for Evidence Based Medicine, 2011.

*Evidence from meta-analysis of randomised controlled trial.

†Evidence from non-randomised controlled cohort studies.

	Dexamphetamine	Elvanse (Shire, Elvanse (Shire, UK)	Methylphenidate				Atomoxetine
			Ritalin (Novartis, Switzerland) or methylphenidate hydrochloride	Medikinet XL (Medice, Germany)	Equasym XL (UCB Pharma, Belgium)	Concerta XL Janssen-Cilag, USA)	(Strattera; Eli Lilly, USA)
Formulation	Tablet	Capsule, dissolvable	Tablet*	Capsule†	Capsule‡	Tablet	Capsule
Immediate release: extended release ratio of methylphenidate			100% immediate release	50% immediate release, 50% extended release	30% immediate release, 70% extended release	22% immediate release, 78% extended release	
Approximate duration of action (hours)	4	13	4	8	8	12	24
Titration, starting dose	2.5 mg 2-3 times a day	30 mg	5 mg 1-2 times a day	5-10 mg	10 mg/day	18 mg/day	<70 kg 0.5 mg/kg/day for 7 days
Titration, weekly increase	5 mg a day	20 mg	5-10 mg	10 mg	10 mg	9-18 mg	As much as 1.2 mg/kg/day
Equivalent daily dose of 30mg methylphenidate hydrochloride	15 mg		30 mg	30 mg	30 mg	36 mg	NA, must follow atomoxetine protocol
Frequency of dose/day	2-3	1	2-3	1	1	1	1 or 2 divided doses
Maximum licensed dose/day	20 mg	70 mg	60 mg	60 mg	60 mg	54 mg	<70 kg, 1.8 mg/kg/day
Controlled drug	Yes	Yes	Yes	Yes	Yes	Yes	No
Approximate cost for 30 tablets (UK 2015 rates)	£26 (5 mg)	£62 (30 mg)	£5.50 (10 mg)	£25 (10 mg)	£25 (10 mg)	£31 (18 mg)	£67 (10 mg)
Other		Licensed in Europe for those with inadequate response to methylphenidate				Continuation license for adult use	

Table 2| Drugs and dosage for treating attention-deficit/hyperactivity disorder (ADHD)⁸⁶

*Can be crushed, put in water, and drunk straight away.

†Can be sprinkled over tablespoon of apple sauce or yogurt (then swallowed without chewing).

‡Can be sprinkled over tablespoon of apple sauce (then swallowed without chewing).

For personal use only: See rights and reprints http://www.bmj.com/permissions

Table 3| How to manage different drugs for attention-deficit/hyperactivity disorder (ADHD)

Drug	General comments	How to start	How to change and stop
Short acting methylphenidate	Allows greatest flexibility to adjust the drug to the needs of children over the course of a day. Administering the drug away from home can be difficult. Parents can top-up with additional doses at their discretion; for example, when children attend clubs after school	Younger children could start on a single morning dose of 5 mg, with gradual dose increases until a response is observed. The same process can then be started for the afternoon dose, as different doses are often needed throughout the day	Can do a straight swap to closest equivalent dose of long acting (usually to lower of two doses if a choice exists). Relatively simple to stop as can reduce doses quickly, with higher doses needing to be tailed off.
Long acting methylphenidate	Preparations can cover the school day and are simpler as they do not need to be taken at school and might improve compliance in older children. Can cover just the school day or longer, depending on which preparation chosen	Often first line treatment with older children to avoid the complexities of adjusting doses (which can negatively impact on compliance). Treatment should start at the lowest possible dose and be reassessed weekly to fortnightly	Straight swap possible to closest equivalent dose from short to long acting (lower dose if choice exists). Relatively simple to stop as can lower doses quickly, with higher doses needing to be tailed off
Atomoxetine	Can be considered if preferred by parents or child or if psychostimulants are contraindicated. It can take longer to exert a beneficial effect and can adversely affect mood	If changing from methylphenidate, ideal to reassess baseline ADHD symptoms and side effects that might have been attributed to methylphenidate by stopping drug for at least two weeks. Can gather useful information on classroom functioning if change made during school term. Can dovetail with methylphenidate if symptoms cannot be tolerated without any drugs	Can slowly reduce by taking drug on alternate days or reducing the dose over 2-4 weeks depending on the length of time it has been taken and the dose

125

Figures



Fig 1 Possible developmental impacts of attention-deficit/hyperactivity disorder



Fig 2 How to assess children for attention-deficit/hyperactivity disorder

126

Per ricevere la newsletter iscriversi al seguente indirizzo: http://crc.marionegri.it/bonati/adhdnews/subscribe.html

Iniziativa nell'ambito del Progetto di Neuropsichiatria dell'Infanzia e dell'Adolescenza (Delibera n. 406 - 2014 Progetti NPI) Il Progetto è realizzato con il contributo, parziale, della Regione Lombardia (in attuazione della D.G. sanità n. 3798 del 08/05/2014) Capofila Progetto: UONPIA Azienda Ospedaliera "Spedali Civili di Brescia" *"Percorsi diagnostico-terapeutici per l'ADHD*".

> IRCCS ISTITUTO DI RICERCHE FARMACOLOGICHE MARIO NEGRI DIPARTIMENTO DI SALUTE PUBBLICA Laboratorio per la Salute Materno Infantile Via Giuseppe La Masa, 19 - 20156 Milano MI - Italia - www.marionegri.it tel +39 02 39014.511 - fax +39 02 3550924 - mother_child@marionegri.i