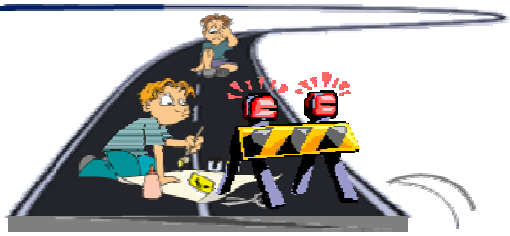
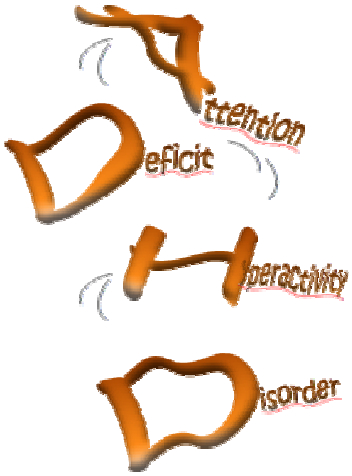
NEWSLETTER





INDICE:

MARIONEGRI
ISTITUTO DI RICERCHE FARMACOLOGICHE

BIBLIOGRAFIA ADHD AGOSTO 2012

Acta Paediatr Int J Paediatr. 2012;101:e431-e433.
RELATIONSHIP BETWEEN ATTENTION-DEFICIT/HYPERACTIVITY DISORDER AND TRANS FATTY ACIDS INTAKE IN FEMALE ADOLESCENTS.
Kim JH, Nam CM, Kim JW, et al.

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Acta Psychiatr Scand. 2012. [in press]
EFFECTS OF TRYPTOPHAN DEPLETION ON REACTIVE AGGRESSION AND AGGRESSIVE DECISION-MAKING IN YOUNG PEOPLE WITH ADHD.
Kotting WF, Bubenzer S, Helmbold K, et al.
Objective: The neurotransmitter serotonin (5-HT) has been linked to the underlying biological processes related to aggressive behaviour. However, only a few studies on this subject involving young people have been published so far.
Method: We aimed to investigate the effects of acute tryptophan depletion (ATD) on reactive aggression and decision-time for aggressive responses in a sample of young people with Attention deficit hyperactivity disorder (n=20), a population at risk for aggressive behaviour. The study design was a double-blind within-subject crossover design. Aggression was assessed using a Point subtraction aggression game (PSAG) with high (HP) and low provocation (LP) trials 2.5h after the intake of ATD and a tryptophan-balanced control condition.
Results: A chi-square comparison was used to identify the effect of ATD on increased aggression after LP. Boys were more likely to respond with an increased aggressive response after HP under ATD as represented by an increased relative risk and odds ratios. Girls had a higher relative risk than boys of an increased point subtraction under ATD after LP. No significant gender differences in decision-time were detected.
Conclusion: An effect of ATD on increased aggression was found in the whole sample after LP. Research involving larger samples is needed to confirm the present preliminary findings.

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

Act Nerv Super Rediviva. 2010;52:193-99.

INCREASED FRACTIONAL ANISOTROPY IN WHITE MATTER OF THE RIGHT FRONTAL REGION IN CHILDREN WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER: A DIFFUSION TENSOR IMAGING STUDY.

Li Q, Sun J, Guo L, et al.

Abnormalities of frontal white matter (WM) have been found in some children with ADHD. The purpose of this study was to explore the changes in WM in child patients with ADHD by DTI, which detects changes in WM microstructure based on properties of diffusion. We also expect to investigate the relationship between the changes in WM and executive function in child patients with ADHD. DTI was performed on 24 patients with ADHD and 20 healthy controls. A series of neuropsychological tests and a structural interview were conducted to assess the cognitive functions and clinical data of the ADHD patients and controls. Firstly, child patients with ADHD have higher fractional anisotropy (FA) values in WM in the right frontal region. Secondly, FA in right frontal WM is positively correlated with scores in the Stroop test.

Conclusions: Increased FA of right frontal WM implies a higher degree of myelination and lower degree of neural branching in WM, contributing to the neurological deficits of ADHD.

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Act Nerv Super Rediviva. 2011;53:45-48.

METHYLPHENIDATE AND GROWTH IN ADHD CHILDREN.

Ptacek R, Kuzelova H.

Attention deficit hyperactivity disorder (ADHD) is a group of developmental disorder characterized by developmentally-inappropriate levels of over activity, inattention and impulsivity. The most common treatment of ADHD is medication with stimulants, by specific methylphenidate which has been shown to improve attention and behavior. The treatment by stimulants may be accompanied by side effects from among decrease of appetite or changes in body development as growth suppression and loss of weight. Many studies describe growth or weight changes only associated with medical treatment of children ADHD. However changes in development and growth can also appear independently on medication. The authors of this paper review the relation of methylphenidate and growth in ADHD children in the current scientific literature.

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Alcohol Clin Exp Res. 2012;36:1431-41.

EXECUTIVE FUNCTION PREDICTS ADAPTIVE BEHAVIOR IN CHILDREN WITH HISTORIES OF HEAVY PRENATAL ALCOHOL EXPOSURE AND ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.

Ware AL, Crocker N, O'Brien JW, et al.

Background: Prenatal exposure to alcohol often results in disruption to discrete cognitive and behavioral domains, including executive function (EF) and adaptive functioning. In the current study, the relation between these 2 domains was examined in children with histories of heavy prenatal alcohol exposure, nonexposed children with a diagnosis of attention-deficit/hyperactivity disorder (ADHD), and typically developing controls.

Methods: As part of a multisite study, 3 groups of children (8 to 18 years, M = 12.10) were tested: children with histories of heavy prenatal alcohol exposure (ALC, n = 142), nonexposed children with ADHD (ADHD, n = 82), and typically developing controls (CON, n = 133) who did not have ADHD or a history of prenatal alcohol exposure. Children completed subtests of the Delis-Kaplan Executive Function System (D-KEFS), and their primary caregivers completed the Vineland Adaptive Behavior Scales-II. Data were analyzed using regression analyses.

Results: Analyses showed that EF measures were predictive of adaptive abilities, and significant interactions between D-KEFS measures and group were present. For the ADHD group, the relation between adaptive abilities and EF was more general, with 3 of the 4 EF measures showing a significant relation with adaptive score. In contrast, for the ALC group, this relation was specific to the nonverbal EF measures. In the CON group, performance on EF tasks did not predict adaptive scores over the influence of age.

Conclusions: These results support prior research in ADHD, suggesting that EF deficits are predictive of poorer adaptive behavior and extend this finding to include children with heavy prenatal exposure to alcohol. However, the relation between EF and adaptive ability differed by group, suggesting unique patterns of abilities in these children. These results provide enhanced understanding of adaptive deficits in these populations, as well as demonstrate the ecological validity of laboratory measures of EF.

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Am J Epidemiol. 2012;176:261-68.

MATERNAL AND PATERNAL SMOKING DURING PREGNANCY AND RISK OF ADHD SYMPTOMS IN OFFSPRING: TESTING FOR INTRAUTERINE EFFECTS.

Langley K, Heron J, Smith GD, et al.

Maternal smoking during pregnancy is associated with attention deficit hyperactivity disorder (ADHD) in offspring. It is assumed by many that this association is causal. Others suggest that observed associations are due to unmeasured genetic factors or other confounding factors. The authors compared risks of maternal smoking during pregnancy with those of paternal smoking during pregnancy. With a causal intrauterine effect, no independent association should be observed between paternal smoking and offspring ADHD. If the association is due to confounding factors, risks of offspring ADHD should be of similar magnitudes regardless of which parent smokes. This hypothesis was tested in 8,324 children from a well-characterized United Kingdom prospective cohort study, the Avon Longitudinal Study of Parents and Children (data from 1991-2000). Associations between offspring ADHD and maternal and paternal smoking during pregnancy were compared using regression analyses. Offspring ADHD symptoms were associated with exposure to both maternal and paternal smoking during pregnancy (mothers: (beta) 0.25, 95 confidence interval: 0.18, 0.32; fathers: (beta) 0.21, 95 confidence interval: 0.15, 0.27). When paternal smoking was examined in the absence of maternal smoking, associations remained and did not appear to be due to passive smoking exposure in utero. These findings suggest that associations between maternal smoking during pregnancy and child ADHD may be due to genetic or household-level confounding rather than to causal intrauterine effects.

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Arch Dis Child. 2012;97:755-58.

SHOULD STIMULANTS BE ADMINISTERED TO MANAGE DIFFICULTIES WITH ATTENTION, HYPERACTIVITY AND IMPULSIVITY FOLLOWING PAEDIATRIC ACQUIRED BRAIN INJURY?

Harvey DW, Morrall MCHJ, Neilly E, et al.

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Asian J Psychiatry. 2012.

ENURESIS AMONG CHILDREN WITH INATTENTIVE ADHD-A POTENTIAL MARKER FOR A DISTINCT SUB-GROUP.

Raghavan S, Mahadevan S, Kattimani S.

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BMC Psychiatry. 2012;107.

NEUROFEEDBACK FOR THE TREATMENT OF CHILDREN AND ADOLESCENTS WITH ADHD: A RANDOMIZED AND CONTROLLED CLINICAL TRIAL USING PARENTAL REPORTS.

Duric NS, Assmus J, Gundersen DI, et al.

Background: A randomized and controlled clinical study was performed to evaluate the use of neurofeedback (NF) to treat attention-deficit/hyperactivity disorder (ADHD) in children and adolescents.

Methods: The ADHD population was selected from an outpatient clinic for Child and Adolescent Mental Health in Norway. Ninety-one of the 275 children and adolescents ranging in age from 6 to 18 years (10.5 years) participated in 30 sessions of an intensive NF program. The reinforcement contingency was based

on the subjects[RIGHT SINGLE QUOTATION MARK] production of cortical beta1 activity (15[EN DASH]18 Hz). The ADHD participants were randomized into three groups, with 30 in the NF group, 31 controls in a group that was given methylphenidate, and 30 in a group that received NF and methylphenidate. ADHD core symptoms were reported by parents using the parent form of the Clinician[RIGHT SINGLE QUOTATION MARK]s Manual for Assessment by Russell A. Barkley.
Results: Ninety-one children and adolescents were effectively randomized by age, sex, intelligence and distribution of ADHD core symptoms. The parents reported significant effects of the treatments, but no significant differences between the treatment groups were observed.
Conclusions: NF was as effective as methylphenidate at treating the attentional and hyperactivity symptoms of ADHD, based on parental reportsTrial registration: Current Controlled Trials NCT01252446.

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BMC Psychiatry. 2012;12.

THE RELATIONSHIP BETWEEN ATTENTION DEFICIT HYPERACTIVITY DISORDER AND PREMATURE INFANTS IN TAIWANESE: A CASE CONTROL STUDY.

Chu SM, Tsai MH, Hwang FM, et al.

Background: Preterm survivors from the neonatal intensive care unit (NICU) are considered to be at risk for some neurobehavioral disorders such as attention-deficit/hyperactivity disorder (ADHD). The current study aimed to explore the relationship between ADHD and premature infants in Taiwan.
Methods: A total of 195 children (157 males and 38 females) diagnosed with ADHD based on DSM-IV and aged between 6 to 12 years and a control group of 212 (164 males, 48 females) age- and sex-matched healthy children were enrolled. The ADHD-Rating scale and CGI severity were performed by child psychiatrists. Demographic data of the children, including birth history, perinatal neurological and respiratory problems were collected to facilitate the investigation of whether a correlation exists between ADHD and prematurity.
Results: The ADHD group had a significantly higher rate of prematurity and significantly higher rate of low birth body weight (defined as <2500 g) than the control group (both P = 0.003). Pearson correlation showed a significantly negative correlation between gestational age and ADHD-RS score, inattentive score, hyperactivity and CGI-S score (P = 0.004, 0.013, 0.015 and 0.002, respectively). However, only a CGI-S score (P = 0.018) showed a significantly correlation between low birth weight and ADHD.
Conclusions: Premature infants have significantly more severe symptoms of ADHD at school age and they were highly correlated. Further study is necessary to determine the main effect and pathogenesis of moderate as well as extreme preterm birth on the development of ADHD.

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BMJ (Online). 2012;345.

CARDIOVASCULAR SAFETY OF CENTRAL NERVOUS SYSTEM STIMULANTS IN CHILDREN AND ADOLESCENTS: POPULATION BASED COHORT STUDY.

Winterstein AG, Gerhard T, Kubilis P, et al.

Objectives: To evaluate the cardiac safety of central nervous system stimulants in children and adolescents.
Design: Population based retrospective cohort study.
Setting: Automated healthcare claims data from 1 219 847 children and young people eligible for 28 state Medicaid programmes from 1999 to 2006 linked to the Social Security Death Master File and the National Death Index.
Participants: Children and young people age 3-18 entered the cohort at the first diagnosis of a mental health condition commonly treated with stimulants (such as attention-deficit/hyperactivity disorder) after a minimum period of six months' eligibility and were followed until loss of eligibility, their 19th birthday, admission to hospital for longer than 30 days, or death. Exclusion criteria included transplant recipients, receipt of dialysis, or claims indicating substance misuse. We retained high risk groups with similar use of stimulants as low risk children (such as children with congenital heart disease). Sociodemographic characteristics, cardiac risk factors, and psychiatric diagnoses obtained from before the index period were

summarised with a propensity score. We used discrete survival analysis to estimate the relative risk for periods of stimulant use and non-use, adjusted for propensity score and antipsychotic use for the full cohort and the high risk and low risk groups.
Main outcome measures: Composite endpoint of stroke, acute myocardial infarction, or sudden cardiac death; a secondary composite endpoint added ventricular arrhythmia
Results: A total of 66 (95 including ventricular arrhythmia) events occurred during 2 321 311 years of follow-up. The odds ratio adjusted for propensity score and antipsychotic use for current versus no stimulant use was 0.62 (95% confidence interval 0.27 to 1.44), with a corresponding adjusted incidence rate of 2.2 and 3.5 per 100 000 patient years for current stimulant and non-use, respectively. Twenty six events occurred in high risk patients (incidence rate 63 per 100 000 patient years) with an odds ratio of 1.02 (0.28 to 3.69). Odds ratios for the secondary endpoint were similar to those for the primary endpoint (0.74, 0.38 to 1.46).
Conclusions: Treatment of children with central nervous stimulants is not significantly associated with an increase in the short term risk of severe cardiac events. Analyses cannot be generalised to children with long term use of stimulants. Furthermore, long term effects of slight increases in heart rate or blood pressure are unknown.

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Can J Psychiatry. 2012;57:93-101.
PREVALENCE OF PRESCRIBED ATTENTION-DEFICIT HYPERACTIVITY DISORDER MEDICATIONS AND DIAGNOSIS AMONG CANADIAN PRESCHOOLERS AND SCHOOL-AGE CHILDREN: 1994-2007.
Brault MC, Lacourse E.
Objective: To describe trends in the prevalence of prescribed attention-deficit hyperactivity disorder (ADHD) medication by Canadian preschoolers and school-age children and to compare these with trends in the prevalence of the ADHD diagnosis between 1994 and 2007.
Methods: Subjects participated in the National Longitudinal Survey on Children and Youth, a Canadian prospective survey collecting data biennially. Three cross-sectional samples of nonreferred children, aged 3 to 9 years and representative of Canadian children for 1994-1995 (n = 12 595), 2000-2001 (n = 13 904), and 2006-2007 (n = 14 655), were selected for the analyses. Information on prescribed medications and ADHD diagnosis was reported by each child's parents. Prevalence was estimated at each cycle, taking the child's age and sex into account.
Results: The estimated prevalence of prescribed medications and ADHD diagnosis in Canada was generally low (less than 3%), but higher for boys (less than 4%) and school-age children (less than 5%). Preschoolers' prevalence of both prescribed medications and ADHD diagnosis stayed stable between 1994 and 2007 (1% or less), while that of school-age children increased nearly 2-fold. Boys' prevalence was higher than that of girls, but girls show the steepest increase over time, up to 2.1-fold. The association between prescribed medications and ADHD diagnosis has strengthened during the 2000s: a greater number of medications were used for children with ADHD (from 43% in 2000 to 59% in 2007) while off-label use of prescribed medications decreased among school-age children.
Conclusions: The upward trend in the prevalence of prescribed ADHD medications and ADHD diagnosis currently observed in contemporary societies is also occurring in Canada, except with preschoolers.

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Child Psychiatry Hum Dev. 2012 Aug;43:523-32.
CHARACTERISTICS OF DSM-IV ATTENTION DEFICIT HYPERACTIVITY DISORDER COMBINED AND PREDOMINANTLY INATTENTIVE SUBTYPES IN A TURKISH CLINICAL SAMPLE.
Oner O, Oner P, Cop E, et al.
Consecutively referred subjects (N=537) to an outpatient clinic were evaluated to compare the Attention Deficit Hyperactivity Disorder Combined (ADHD-C) and predominantly inattentive (ADHD-PI) subtypes using parent and teacher ratings and neuropsychological variables. Statistical significance was at P<0.002 adjusted for multiple comparisons. ADHD-PI subjects were older, more likely to be female, higher socioeconomic status, had lower Child Behavior Checklist and Teacher Report Form Aggression,

Delinquency and Social Problems scores, and higher Withdrawal and Competence scores, compared to ADHD-C subjects. Comorbid conduct problems were more common among ADHD-C subjects. There were no differences in terms of anxiety/depression, and neuropsychological measures. The study is unique in that it provides data on a broad range of measures from a middle income developing country with important confirmation of similar pattern of differences and similarities between ADHD-C and ADHD-PI subtypes previously reported in North American and Western European samples.

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Clin Neurophysiol. 2012;123:e82.

EPILEPTIFORM ABNORMALITIES IN CHILDREN AT ADHD ASSESSMENT AND AT 4 YEARS FOLLOW-UP.

Socanski D, Herigstad A.

There are some relationships between attention-deficit/hyperactivity disorder (ADHD), ADHD symptoms and interictal epileptiform abnormalities (EA) on EEG.

Purpose: To investigate whether EA recorded at the time of ADHD assessment influence on epileptic seizures (ESz) occurrence during 4 years follow-up.

Methods: A retrospective study of 607 ADHD children (82.4% male), aged between 5 and 14 years, who were diagnosed between January 2000 and December 2005. At least one routine EEG was performed in 517 patients, 14 of them had previous history of epilepsy. The 27 patients with EA and without epilepsy were followed-up for 4 years.

Measure outcomes were: the ESz occurrence and the persistence of EA.

Results: Among 27 patients with EA at baseline, five had some symptoms suggestive for ESz. At follow-up 4 years later none of these 27 patients had developed ESz. EA disappeared on the control EEG in the majority of patients. EA in ADHD children without epilepsy co-morbidity do not necessarily suggest an increased seizure risk and a careful diagnostic consideration is warranted.

Conclusions: EA occur more often in children with ADHD regardless of the previous history of epilepsy. A careful diagnostic consideration is needed in order not to overestimate the temporarily occurrence of EA during the ADHD assessment.

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Clin Pediatr. 2012;51:763-69.

WHY DO CHILDREN WITH ADHD DISCONTINUE THEIR MEDICATION?

Toomey SL, Sox CM, Rusinak D, et al.

Objective. To examine factors associated with parent-reported discontinuation of attention-deficit/hyperactivity disorder (ADHD) medication.

Methods. The authors conducted a telephone survey of parents of children 6 to 18 years old who had recently initiated ADHD medication according to insurance claims.

Results. A total of 127 parents of children with ADHD who had recently initiated ADHD medication completed the survey (43% response rate); 21% discontinued the ADHD medication. Parents of discontinuers were less likely to report having discussed the risks and benefits of ADHD medication with primary care providers (59% vs 82%, P = .03) and were more likely to report psychological side effects (58% vs 21%, P (greater-than or equal to) .001). Multivariate analyses demonstrated that both psychological side effects and perceived inadequate medication effectiveness were associated with discontinuation.

Conclusions. Many children discontinue ADHD medication within the first year, often because of psychological side effects or perceived inadequate medication effectiveness. Improved methods for psychological side effect management, setting realistic medication goals, and assessing therapeutic success are needed.

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Clin Psychol Rev. 2012;32:605-17.

MODERATORS OF WORKING MEMORY DEFICITS IN CHILDREN WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER (ADHD): A META-ANALYTIC REVIEW.

Kasper LJ, Alderson RM, Hudec KL.

Working memory has assumed a prominent role as a primary neurocognitive deficit or endophenotype in extant models of attention-deficit/hyperactivity disorder (ADHD). The current study updated previous reviews and employed meta-analytic techniques to examine a broad range of moderating variables of effect size heterogeneity across phonological and visuospatial working memory tasks. Collectively, results revealed large between-group effect sizes across both working memory domains. In addition, several sample (percent female) and task (number of experimental trials, recall vs. recognition tasks, and demands on the central executive) moderating variables explained significant effect size variability among phonological and visuospatial studies. These findings suggest that children with ADHD exhibit statistically significant, large magnitude working memory deficits relative to their typically developing peers.

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Clin Toxicol. 2012;50:606-07.

A RETROSPECTIVE REVIEW OF SUPRATHERAPEUTIC ADHD MEDICATION INGESTIONS IN PEDIATRIC PATIENTS.

Lo JC, Vo T, Cortez-Gomez B, et al.

Objective: Approximately 3% of American children receive attention defi cit hyperactivity disorder (ADHD) medications, including stimulants, alpha 2 agonists, and antidepressants. Thousands of patients present to health care facilities (HCF) annually for supratherapeutic consumption of ADHD medications. The purpose of this study is to better understand the characteristics of supratherapeutic ADHD medication exposures in pediatric patients.

Methods: For this study, we queried the electronic database of a statewide poison system - for cases from Jan 2006 to Dec 2010, for patients 18 years old and under, using the following search terms: methylphenidate, dexmethylphenidate, amphetamine, lisdexamfetamine, atomaxetine, clonidine, and guanfacine. An Excel spreadsheet was used to record the following variables: age, sex, substances ingested, sustained release (SR) preparation or not, dose of exposure, co-ingestants, where the ingestion occurred, reason for exposure (taking additional dose, given additional dose, taking sibling's meds, dispensing error), symptoms, duration of symptoms, HCF evaluation, admit vs discharge, length of hospitalization, treatment, and number of follow up.

Results: 301 cases of pediatric patients who consumed supratherapeutic amounts of ADHD medications were reported. The most common age of ingestions were 6 to 10 years (N-26-35). The top 3 reported ADHD substances ingested were methylphenidate 28 (42.5%), amphetamine/dextroamphetamine-55 (18.3%), and clonidine-52 (17.3%). 161 were SR formulations. The dose ranged from 0.5 to 10 tablets. Co-ingestion was reported in 78 patients. The ingestion occurred at home in 298 cases and school in 3 cases. Reason for exposure included taking additional dose-103 (34.2%), given additional dose-145 (15%), taking sibling's meds-28 (9.3%), dispensing error-25 (8.3%). Symptoms were recorded in 92 (30.6%) patients with the top 3 symptoms: lethargy 39 (13%), tachycardia-21 (7%), hypotension-19 (6.3%). 120 patients (40%) were evaluated in HCF. Of these, 29 were admitted for 1 day or less. Alpha agonists result in more HCF visits and symptoms. Treatment included AC-28 (9.3%), IV fluid-9 (3%), and benzodiazepine-3 (1%).

Conclusions: The most commonly reported ADHD medications taken were methylphenidate and amphetamine/dextroamphetamine. Thirty percent of patients had reported symptoms. Alpha 2 agonists result in more HCF visits and symptoms. Most pediatric patients with supratherapeutic ingestions of ADHD, excluding alpha 2 agonists, do not require HCF visits.

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Curr Psychiatry Rep. 2012;1-9.

EMERGING SUPPORT FOR A ROLE OF EXERCISE IN ATTENTION-DEFICIT/HYPERACTIVITY DISORDER INTERVENTION PLANNING.

Berwid OG, Halperin JM.

Recent years have seen an expansion of interest in non-pharmacological interventions for attention-deficit/hyperactivity disorder (ADHD). Although considerable treatment development has focused on cognitive training programs, compelling evidence indicates that intense aerobic exercise enhances brain structure and function, and as such, might be beneficial to children with ADHD. This paper reviews evidence for a direct impact of exercise on neural functioning and preliminary evidence that exercise may have positive effects on children with ADHD. At present, data are promising and support the need for further study, but are insufficient to recommend widespread use of such interventions for children with ADHD.

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Curr Psychiatry Rep. 2012;1-7.

CURRENT STATUS OF NEUROFEEDBACK FOR ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.

Lofthouse N, Arnold LE, Hurt E.

As conventional treatments offer incomplete benefit for over 33 % of children with attention-deficit/hyperactivity disorder (ADHD) and many refuse to try them, additional treatments are needed. One of the most promising is neurofeedback (NF, EEG biofeedback), which trains the brain with real-time video/audio information about its electrical activity measured from scalp electrodes. Since 2010, data from 8 randomized controlled studies of NF have been published with overall mean effect sizes of: 0.40 (all measures), 0.42 (ADHD measures), 0.56 (inattention), and 0.54 (hyperactivity/ impulsivity). Unfortunately, the benefit reported from randomized studies has not been observed in the few small blinded studies conducted. Main study strengths include randomization, evidence-based diagnostic assessments, multi-domain treatment outcomes, use of some type of blinding, and sham control conditions. Main study limitations include lack of large samples, abnormal EEG participant selection, double-blinding, and testing of blind validity and sham inertness. Most recently, a collaborative NF research group has been planning a definitive double-blind well-controlled trial.

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Dev Med Child Neurol. 2012;54:68-69.

RELATIONSHIP OF ATTENTION-DEFICIT-HYPERACTIVITY DISORDER AND SLEEP DISORDERS: AN EVENT-RELATED POTENTIAL STUDY USING THE POSNER PARADIGM.

Cheong PL, Gau SF, Lee WT.

Objective: Our objective was to study event-related potentials (ERP) in children with attention-deficit-hyperactivity disorder (ADHD), with or without sleep problems, in children with sleep problems only and in normal children, to investigate the relationship of ADHD and sleep problems.

Design: Prospective cohort study.

Method: Children aged 6-12 years were recruited for the four groups described above. Children were included with IQ <80 or underlying neuropsychiatric or developmental disabilities. Combined analysis of electrophysiological components [P1, N2, P3, contingent negative variation (CNV)] and behavioral data [reaction time (RT) and the error percentage] were done using repeated measures analysis of variance (ANOVA) and Fisher's least significance test for multiple comparisons, using SAS version 9.1.

Results: Our participants with ADHD and sleep problems had the longest mean reaction time and most anticipation errors, suggesting greater impulsivity, poorer attention orienting and probably poorer coordination. Those with sleep problems had similar behavioral performance as controls, but the smallest ERP components. There was a smaller increment in the target-P1 amplitudes from valid to invalid condition in ADHD groups (22.7% and 31%) compared with non-ADHD groups (49% and 58%), suggesting poorer function in attention shifting in ADHDparticipants.

Conclusion: Though participants with sleep problems showed similar behavioral performances as the controls, their ERP measurements were poorer than controls and seemed similar to those with ADHD and

sleep problems. The ADHD patients with sleep problems might have more severe executive deficits than those with ADHD only and thus they might need more attention and aggressive intervention including behavioral therapy and stimulants.

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Dev Med Child Neurol. 2012;54:4.

IRON DEFICIENCY ANAEMIA (IDA) IN CHILDREN WITH ADHD.

Abbas EM, Valli S.

Objective: To determine whether children with ADHD are at risk of Iron deficiency anaemia (IDA).

Methods: We reviewed all case files, electronic records and laboratory results (Serum Iron, Ferritin and Full blood count) of 100 children with ADHD. Forty cases were suspected to have IDA from history and clinical findings. Only 38 cases were included as two blood samples clotted.

Results: Two children were female and 36 male, with ages ranging 4-14 years (median 7y). 92% had ADHD and 8% had Attention Deficit Disorder (ADD) (Figure 1). Fiftyfive percentage had sleeping difficulties, 32% learning difficulties and 13% had Autistic spectrum disorder (Figure 2). Seventeen had poor appetite, two poor weight gain, one food allergy, one nut allergy and eight had significantly reduced appetite on medication (Figure 3). Serum Ferritin was low in 50%, the lower limit for Ferritin being 30lg/ mL in males and 13lg/mL in females in our laboratory. Serum Iron and transferrin saturation were low in 32% and 45% respectively. Full blood count was abnormal in 42%, with MCV low in 40%. (Tables 1-3).

Conclusions: IDA is observed in 8-12% of children in UK. However, in our cohort of children with ADHD, we have observed an increased proportion of IDA. Had we used a higher limit of Ferritin (50lg/mL) as in previous studies, we would have identified even more cases. However larger, well-designed prospective studies are now indicated to study this phenomenon in more detail. It is useful to screen children with ADHD for iron deficiency anaemia and offer treatment.

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Dev Med Child Neurol. 2012;54:21.

PERINATAL COMPLICATIONS AND PSYCHO-SOCIAL OUTCOMES IN CHILDREN WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER.

Adeosun II, Ogun OC, Ijarogbe TG.

Background: Pregnancy and perinatal complications are some of the most common environmental risk factors associated with Attention Deficit Hyperactivity Disorder (ADHD). However the relationship between these risk factors and outcomes of children with ADHD is not completely known.

Methods: This study assessed the relationship between perinatal complications and some psycho-social outcomes in children with ADHD. Patients with ADHD(n=78), attending the Child and Adolescent clinic of the Neuro-Psychiatric Hospital Yaba Nigeria were consecutively recruited. Outcomes assessed include symptom severity, presence of psychiatric co-morbidity and psycho-social functioning using the Vanderbilt ADHD Diagnostic Parent Rating Scale, Columbia Impairment Scale and Children's Global Assessment Scale. Information on the history of perinatal complications was obtained from the mothers of the children, with a standardised interview, blind to the outcome measures.

Results: The majority (68.9%) of the participants were males. Their age ranged from 3 to 16 years (mean age 7.4(plus or minus)3.3yrs). Children with a history of perinatal complications had significantly worse symptom severity (P=0.01), lower psycho-social functioning (P<0.001) and higher rates of psychiatric co-morbidity (P<0.001). After adjusting for confounding factors using regression analysis, history of perinatal complications independently predicted worse outcomes in the children.

Discussion: Perinatal complications negatively impact on the psychosocial outcomes of children with ADHD. Children with ADHD who have a history of perinatal complications may constitute a more vulnerable sub-group that could benefit from certain targeted interventions.

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Dev Med Child Neurol. 2012;54:19-20.

COGNITIVE CORRELATES OF ADHD SYMPTOMS IN PRESCHOOL CHILDREN.

Thomaidis L, Mantoudis S, Critselis E, et al.

Objective: To examine the association between attention deficit hyperactivity disorder (ADHD) and cognitive skills among preschool children.

Methods: We conducted a cross-sectional study among a representative nationwide sample of preschool children. ADHD was assessed though a structured diagnostic interview based on DSM-III-R criteria to both primary caretakers and teachers. Cognitive skills were assessed though a standardized school readiness screening test (A' Test). We used the Mantel-Haenszel method to compare the cognitive skills of preschoolers with and without ADHD.

Results: Among the study population (n=4480) the occurrence of ADHD approximated 4.6% (n=205). These were significantly more likely to present abnormal scores for critical reasoning skills (OR=5.51; 95% CI: 3.41-8.90), organizational skills (OR=3.67; 95% CI: 2.54-5.29), visual motor skills (OR=3.33; 95% CI: 2.39-4.63), visual perception skills (OR=3.22; 95% CI: 1.83-5.66), language skills (OR=2.68; 95% CI: 1.76-4.10), and abstract thinking skills (OR=2.50; 95% CI: 1.64-3.83).

Conclusions: Preschool children with ADHD run into a notable high risk of compromised cognitive skills. Timely testing and early interventions may optimize the above difficulties and enhance school performance.

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Dev Med Child Neurol. 2012.

THE ADVERSE INFLUENCE OF ATTENTION-DEFICIT DISORDER WITH OR WITHOUT HYPERACTIVITY ON COGNITION IN NEUROFIBROMATOSIS TYPE 1.

Lidzba K, Granstrom S, Lindenau J, et al.

Aim A substantial proportion of patients with neurofibromatosis type 1 (NF1) have attention-deficit disorder with or without hyperactivity (AD[H]D). This study explored the influence of AD(H)D symptoms on the intellectual profile of patients with NF1.

Method We retrospectively analysed neuropsychological data from 114 children (66 males, 48 females; age range 6-16y; mean age 9y 3mo [SE 3mo]) with NF1 from an NF1 outpatients department. Assessment included psychiatric diagnosis of AD(H)D (DSM-IV-TR criteria) and intelligence testing (Wechsler Intelligence Scale for Children, German version). Magnetic resonance images were available for all patients, intracranial findings being an exclusion criterion. The effects of AD(H)D symptoms on intelligence and on the cognitive profile were tested by analyses of variance.

Results Patients with AD(H)D symptoms performed significantly worse than those without AD(H)D symptoms on all intelligence measures (main effects for Full-scale, Verbal, and Performance IQ; $p<0.005$). Subtests typically impaired in patients with NF1 (visuospatial skills and arithmetic) were not specifically influenced by AD(H)D symptoms. There were no differences between AD(H)D subtypes.

Interpretation AD(H)D symptoms have a negative impact on the intellectual development of children with NF1. This impact seems to be of an unspecific nature, with a general attenuation of the cognitive profile. Please also see the Commentary on this paper by Huijbregts .

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Dev Med Child Neurol. 2012;54:69.

ASSOCIATION BETWEEN ALLERGIC DISEASES AND ATTENTION-DEFICIT-HYPERACTIVITY DISORDER IN CHILDHOOD: A POPULATION-BASED STUDY.

Tsai JD, Lue KH.

Objective: Both allergic diseases and attention-deficithyperactivity disorder (ADHD) are common paediatric disorders that may lead to learning and sleep problem. Reports concern the linkage between allergy and ADHD remains limited. We performed a matched case-control study to evaluate correlations between allergic diseases and ADHD in childhood.

Design: Matched case-control study.

Method: A National Health Insurance database in Taiwan was used to identify children with ADHD and to randomly select controls from the period 2002 to 2009. Unconditional logistic regression estimated odds

ratios (ORs) and 95% confidence intervals (CIs) of the association between allergic diseases, the number of allergic comorbidities, and ADHD.
Results: A total of 4692 children with ADHD and 18 768 controls were enrolled. The majority (77.9%) of incident ADHD cases were boys; 6.9% aged 1-5 years, 70.1% aged 6-11 years and 23% aged 12-18 years. ADHD was highly correlated with allergic diseases. The corresponding ORs were 1.81 [95% confidence interval (CI)=1.69-1.93] and 1.69 (95% CI=1.58-1.81), respectively. With lower prevalence, children with atopic dermatitis and asthma were also at higher risk of attention-deficit-hyperactivity disorder, with ORs of 1.80 (95% CI=1.58-2.05) and 1.48 (1.24- 1.78). Risk was significantly increased with the number of allergic comorbidities; this trend was positively modified by age (P<0.0001) but equal in both genders.
Conclusion: Most children with ADHD displayed high rates of allergic disease. Risk also increased with the number of allergic comorbidities, urbanization and age. While managing ADHD in childhood, awareness of the comorbidities helps the physician provide better comprehensive management.

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Dev Med Child Neurol. 2012.
COGNITIVE-BEHAVIORAL PHENOTYPE OR COMORBID DISORDER? THE CASE OF ATTENTION-DEFICIT-HYPERACTIVITY DISORDER IN NEUROFIBROMATOSIS TYPE 1.
Huijbregts S.
This commentary is on the original articles by Lidzba etal and Payne et.al.

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Dev Med Child Neurol. 2012;54:93.
ATTENTION-DEFICIT-HYPERACTIVITY DISORDER IN CHILDHOOD AND ADOLESCENCE IS ASSOCIATED WITH INCREASED GRAY MATTER VOLUME IN THE INSULA.
Tomoda A, Mizuno K, Yoneda T.
Objective: Research has addressed the epidemiology and the increasing prevalence of attention-deficit-hyperactivity disorder (ADHD). ADHD is reportedly associated with both global and local morphological changes in the brain. Nevertheless, little is known about grey matter volumes (GMV) in patients with ADHD. An objective overall assessment using voxel-based morphometry (VBM) has yet to be reported in paediatric patients with ADHD. The aim of this study was to explore GMV abnormalities in ADHD in childhood and adolescence.
Design: Control-matched cohort study.
Method: High-resolution T1-weighted MRI datasets were obtained from 39 unmedicated ADHD participants and 39 healthy controls of equivalent age and socioeconomic status, with no history of trauma or other developmental disorder.
Results: GMV was increased by 13.1% in the right insula (P=0.037, corrected) of ADHD participants. The GMV in this region inversely correlated with impulsiveness of the patients (r=-0.321, P=0.049).
Conclusion: A recent fMRI study demonstrated decreased insula activation during attentional avoidance in ADHD participants (Stoy 2011). Our findings provide evidence of the direct involvement of the right insula in the impulsiveness seen in ADHD patients.

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Dev Med Child Neurol. 2012;54:67-68.
ETHNICITY AND ATTENTION-DEFICIT-HYPERACTIVITY DISORDER PREVALENCE IN ASIA.
Sakakihara Y, Anji Y, Tran TD, et al.
Objective: Attention-deficit-hyperactivity disorder (ADHD) is among the most common neuropsychological disorders in childhood. Although there were numerous epidemiologi-cal studies on ADHD, reported prevalence rates were quite diverse. In the present study, we compared the scores of an ADHD rating scale reported by parents in Thailand, Vietnam and Japan to study the ethnic differences of ADHD.

Design: Prospective cohort study.
Method: We selected three geographically distinct regions from three countries, and randomly recruited 5 to 6 year old children from each region. Parents were asked to complete the ADHD Rating Scale (DuPaul) translated into their national languages.
Results: A total of 1108 parents (Japan: 529, Vietnam: 396, Thailand: 183; male children: 580, female children: 528) completed the scale. The average total scores of ADHD in Japan, Vietnam and Thailand were 8.6, 14.7 and 17.0 respectively. The differences were statistically significant (P<0.01, ANOVA). Since it was indicated that inattention score rather than total score was more predictive of clinical diagnosis of ADHD (DuPaul, 1998), we also compared the inattention scores among the three countries. The average inattention scores were 4.6, 6.7 and 8.0, and the differences were also statistically significant (P<0.01).
Conclusion: Although clinical diagnosis is not solely made from parent rated scores, they comprise important information for the diagnosis of ADHD. Further studies are necessary to understand the ethnic differences of in ADHD epidemiology.

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Dev Med Child Neurol. 2012;54:69.
CORTISOL AWAKENING RESPONSE IMPROVES AFTER A SUMMER TREATMENT PROGRAM FOR CHILDREN WITH ATTENTION-DEFICIT-HYPERACTIVITY DISORDER (ADHD).
Yamashita Y, Okamura H, Nagamitsu S, et al.
Objective: Cortisol levels are low in the night but rise in the early hours before waking. After awaking in the morning, most people show a further rise, with the concentration peaking 20-30 minutes later. This phenomenon is termed the 'cortisol awakening response' (CAR). The CAR is associated with stress and health in potentially significant ways. The aim of this study was to examine the CAR in children with attention-deficit-hyperactivity disorder (ADHD) before and after 2 weeks of an intensive summer treatment program (STP).
Design: Prospective intervention study.
Method: The participants were twenty children aged 7-12 years old who participated in an STP in 2009. Saliva samples for cortisol measurement were collected twice, at awakening in the morning and 30 minutes later, both before and two weeks later, after the STP. Twice parents filled out the ADHD Rating Scale-IV (RS-IV) and quality of life (QoL) questionnaire, before and after the STP.
Results: CAR was not observed in children with ADHD before the STP, but it was obvious after the STP (P<0.05). The changes of CAR were positively correlated with the improvement of the inattention score of ADHD RS-IV P<0.05), but no correlation was found between the changes of hyperactivity/impulsivity score and CAR in ADHD RSIV. No significant correlation was found between CAR and QoL scores (P<0.1).
Conclusion: Significant improvement of CAR after STP might suggest reduced stress or better hypothalamicpituitary- adrenocortical function after the STP.

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Epilepsy Curr. 2012;12.
ATTENTION DEFICIT HYPERACTIVITY DISORDER IN DIFFERENT SEIZURE TYPES; PRELIMINARY STUDY.
Kim GH, Eun B, Eun S, et al.
Rationale: Previous reports have suggested that the high prevalence of attention deficit hyperactivity disorder (ADHD) in epileptic children. The purpose of this preliminary study was to investigate whether the prevalence of ADHD in epileptic children is higher even for patients with well controlled epilepsy. Another purpose was to assess the possible relations between different seizure types and ADHD.
Methods: Epileptic children and adolescents, aged 6 to18years, who visited for 6 consecutive months were included in the study. Among them we included only those without significant developmental delay as well as being seizure-free for over 3 months. We utilized parent questionnaires based on DSM-IV criteria to diagnose ADHD and Korean version of Child Behavior Checklist and Child Depression Inventory.
Results: We enrolled 85 patients (mean age, 10.1(plus or minus)2.8) including 44 boys and 41 girls. Eighteen (5.6%) were diagnosed with ADHD (12 combined, 6 inattentive types; 10 boys, 8 girls). The number of ADHD patients varied between the seizure types: childhood or juvenile absence epilepsy

(33.3%, 3 of 9); cryptogenic focal epilepsy (17.6%, 6 of 34); generalized epilepsy (28.6%, 6 of 21); benign rolandic epilepsy (9.5%, 2 of 21). Prevalence of ADHD was significantly high in absence epilepsy (p=0.043).
Conclusions: Contrary to previous reports, the prevalence of ADHD in patients with well controlled epilepsy and without significant develop mental delay is not higher than in the general pediatric population. And the predominant type of ADHD in epileptic children is the combined type, which is the same as in the general pediatric population. Our results also indicate a greater likelihood of ADHD in absence epilepsy even during seizure-free.

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Eur Neuropsychopharmacol. 2012.
EVALUATION OF COMMON VARIANTS IN 16 GENES INVOLVED IN THE REGULATION OF NEUROTRANSMITTER RELEASE IN ADHD.
Sanchez-Mora C, Cormand B, Ramos-Quiroga JA, et al.
Attention-deficit hyperactivity disorder (ADHD) is a neurobehavioral disorder characterized by inappropriate difficulties to sustain attention, control impulses and modulate activity level. Although ADHD is one of the most prevalent childhood psychiatric disorders, it also persists into adulthood in around 30-50% of the cases. Based on the effect of psychostimulants used in the pharmacological treatment of ADHD, dysfunctions in neuroplasticity mechanisms and synapses have been postulated to be involved in the pathophysiology of ADHD. With this background, we evaluated, both in childhood and adulthood ADHD, the role of several genes involved in the control of neurotransmitter release through synaptic vesicle docking, fusion and recycling processes by means of a population-based association study. We analyzed single nucleotide polymorphisms across 16 genes in a clinical sample of 950 ADHD patients (506 adults and 444 children) and 905 controls. Single and multiple-marker analyses identified several significant associations after correcting for multiple testing with a false discovery rate (FDR) of 15%: (i) the SYT2 gene was strongly associated with both adulthood and childhood ADHD (p=0.001, OR=1.49 (1.18-1.89) and p=0.007, OR=1.37 (1.09-1.72), respectively) and (ii) STX1A was found associated with ADHD only in adults (p=0.0041; OR=1.28 (1.08-1.51)). These data provide preliminary evidence for the involvement of genes that participate in the control of neurotransmitter release in the genetic predisposition to ADHD through a gene-system association study. Further follow-up studies in larger cohorts and deep-sequencing of the associated genomic regions are required to identify sequence variants directly involved in ADHD.

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Eur Neuropsychopharmacol. 2012.
LONG-TERM EFFICACY AND SAFETY OF TREATMENT WITH STIMULANTS AND ATOMOXETINE IN ADULT ADHD: A REVIEW OF CONTROLLED AND NATURALISTIC STUDIES.
Fredriksen M, Halmoy A, Faraone SV, et al.
Attention-deficit/hyperactivity disorder (ADHD) is a common disorder of childhood that often persists into adulthood. Although stimulant medications are recommended as the first-line treatment for ADHD because of their documented short-term effects in children and adults, less is known about their effects on long-term outcome in adults. Here we review the long-term efficacy and safety of the stimulant drugs methylphenidate and amphetamine, as well as the related compound atomoxetine. We performed a systematic review to identify direct and indirect effects of stimulant therapy on long-term outcome in adults. Five randomized controlled trials (RCTs), and 10 open-label extension studies of initial short-term RCTs, with total follow-up of at least 24 weeks, were identified. All these RCTs found that medication was significantly more efficacious than placebo in treating ADHD in adults, and the extension studies showed that this favorable effect of medication was maintained during the open-label follow-up period. However, since the maximum duration of these pharmacological trials was 4 years, we also reviewed 18 defined naturalistic longitudinal and cross-sectional studies, to provide more information about longer term functional outcomes, side effects and complications. These observational studies also showed positive correlations between early recognition of the disorder, stimulant treatment during childhood and favorable long-term outcome in adult ADHD patients. In conclusion, stimulant therapy of ADHD has long-term beneficial effects and is well

tolerated. However, more longitudinal studies of long duration should be performed. In addition, the ethical issues involved in performing double blind RCTs of many years duration should be further explored.

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Front Syst Neurosci. 2012.

AUTOMATED DIAGNOSES OF ATTENTION DEFICIT HYPERACTIVE DISORDER USING MAGNETIC RESONANCE IMAGING.

Eloyan A, Muschelli J, Nebel MB, et al.

Successful automated diagnoses of attention deficit hyperactive disorder (ADHD) using imaging and functional biomarkers would have fundamental consequences on the public health impact of the disease. In this work, we show results on the predictability of ADHD using imaging biomarkers and discuss the scientific and diagnostic impacts of the research. We created a prediction model using the land-mark ADHD 200 data set focusing on resting state functional connectivity (rs-fc) and structural brain imaging. We predicted ADHD status and subtype, obtained by behavioral examination, using imaging data, intelligence quotients and other covariates. The novel contributions of this manuscript include a thorough exploration of prediction and image feature extraction methodology on this form of data, including the use of singular value decompositions, CUR decompositions, random forest, gradient boosting, bagging, voxel-based morphometry and support vector machines as well as important insights into the value, and potentially lack thereof, of imaging biomarkers of disease. The key results include the CUR-based decomposition of the rs-fc-fMRI along with gradient boosting and the prediction algorithm based on a motor network parcellation and random forest algorithm. We conjecture that the CUR decomposition is largely diagnosing common population directions of head motion. Of note, a byproduct of this research is a potential automated method for detecting subtle in-scanner motion. The final prediction algorithm, a weighted combination of several algorithms, had an external test set specificity of 94% with sensitivity of 21%. The most promising imaging biomarker was a correlation graph from a motor network parcellation. In summary, we have undertaken a large-scale statistical exploratory prediction exercise on the unique ADHD 200 data set. The exercise produced several potential leads for future scientific exploration of the neurological basis of ADHD.

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Front Syst Neurosci. 2012.

INDIVIDUAL CLASSIFICATION OF ADHD PATIENTS BY INTEGRATING MULTISCALE NEUROIMAGING MARKERS AND ADVANCED PATTERN RECOGNITION TECHNIQUES.

Cheng W, Ji X, Zhang J, et al.

Accurate classification or prediction of the brain state across individual subject, i.e., healthy, or with brain disorders, is generally a more difficult task than merely finding group differences. The former must be approached with highly informative and sensitive biomarkers as well as effective pattern classification/feature selection approaches. In this paper, we propose a systematic methodology to discriminate attention deficit hyperactivity disorder (ADHD) patients from healthy controls on the individual level. Multiple neuroimaging markers that are proved to be sensitive features are identified, which include multiscale characteristics extracted from blood oxygenation level dependent (BOLD) signals, such as regional homogeneity (ReHo) and amplitude of low-frequency fluctuations. Functional connectivity derived from Pearson, partial, and spatial correlation is also utilized to reflect the abnormal patterns of functional integration, or, dysconnectivity syndromes in the brain. These neuroimaging markers are calculated on either voxel or regional level. Advanced feature selection approach is then designed, including a brain-wise association study (BWAS). Using identified features and proper feature integration, a support vector machine (SVM) classifier can achieve a cross-validated classification accuracy of 76.15% across individuals from a large dataset consisting of 141 healthy controls and 98 ADHD patients, with the sensitivity being 63.27% and the specificity being 85.11%. Our results show that the most discriminative features for classification are primarily associated with the frontal and cerebellar regions. The proposed methodology is expected to improve clinical diagnosis and evaluation of treatment for ADHD patient, and to have wider applications in diagnosis of general neuropsychiatric disorders.

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Genet Couns. 2012;23:329-33.

A DE NOVO SUPERNUMERARY MARKER CHROMOSOME DERIVED FROM CHROMOSOME 9P (9P13.1->P23) ASSOCIATED WITH ATTENTION DEFICIT AND HYPERACTIVITY DISORDER.

Chen CP, Lin SP, Su JW, et al.

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Health Qual Life Outcomes. 2012;10.

HEALTH-RELATED QUALITY OF LIFE AMONG CHILDREN WITH MENTAL HEALTH PROBLEMS: A POPULATION-BASED APPROACH.

Dey M, Mohler-Kuo M, Landolt MA.

Background: Children with mental health problems have been neglected in health-related quality of life (HRQOL) studies. Therefore, the aims of the current study were 1) to assess the influence of the presence of mental or physical health problems on HRQOL; and 2) to analyze the effects of item overlap between mental health problems and HRQOL-measurements.

Methods: Proxy- and self-rated HRQOL (KIDSCREEN-27) of children 9-14 years old was assessed across children with mental health problems (n = 535), children with physical health problems (n=327), and healthy controls (n=744). Multiple linear regression analyses were conducted with health status, severity of symptoms, status of medication use, gender and nationality as independent, and HRQOL scores as dependent variables. The effects of item overlap were analyzed by repeating regression analyses while excluding those HRQOL items that contextually overlapped the most frequently-occurring mental health problem (attention deficits).

Results: Severity of symptoms was the strongest predictor of reduced HRQOL. However, all other predictors (except for the status of medication use) also contributed to the prediction of some HRQOL scores. Controlling for item overlap did not meaningfully alter the results.

Conclusions: When children with different health constraints are compared, the severity of their particular health problems should be considered. Furthermore, item overlap seems not to be a major problem when the HRQOL of children with mental health problems is studied. Hence, HRQOL assessments are useful to gather information that goes beyond the clinical symptoms of a health problem. This information can, for instance, be used to improve clinical practice.

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Hong Kong J Paediatr. 2012;17:162-66.

EPIDEMIOLOGIC FEATURE OF ATTENTION DEFICIT AND HYPERACTIVITY DISORDER (ADHD) IN ELEMENTARY SCHOOL CHILDREN.

Namdari P, Nazari H, Pournia Y.

Attention Deficit Hyperactivity Disorder (ADHD) is a prevalent psychiatric disorders starting from childhood that has afflicted 3-5% of school children. ADHD has destructive effects on people's social, educational, personality, and behaviuoral relationships in childhood and adulthood. This cross-sectional school based study included all the students studying in grades one to five at elementary schools in Khorramabad (N=945), Iran. Eight girls and 8 boys schools were selected using a cluster, multi-stage sampling method. The Child Symptom Inventories-4 (CSI4) standardised questionnaire was used to collect the data. The questionnaires were completed by teachers and parents in separate meetings. The cases that showed ADHD underwent clinical examinations by psychiatrists. The results were analysed via descriptive statistics and X2 tests using the SPSS software. Out of 945 children, 50.7% and 49.3% were girls and boys respectively. Among the people studied, 3.17% suffered from ADHD including 40% from attention deficit, 33.3% from hyperactivity, and 26.6% from the combined type. ADHD was more prevalent in boys than in girls (4.9% vs. 1.5%). There was a significant relationship between children's gender and ADHD ($p<0.005$). The students in grade 5 showed the lowest, and those in grades 2 and 3 showed the highest ADHD rates. However, no significant relationships were found between parents' age, educational level, occupation, income, grade, and psychiatric problems in family. Identifying behavioral disorders including ADHD in

school children and adolescents, due to their high prevalence, seems to be necessary. Therefore, this study was conducted to investigate ADHD prevalence in elementary school students of Khorramabad.

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Hum Psychopharmacol. 2012;27:411-18.

BUPROPION VERSUS METHYLPHENIDATE IN THE TREATMENT OF CHILDREN WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER: RANDOMIZED DOUBLE-BLIND STUDY.

Jafarinia M, Mohammadi MR, Modabbernia A, et al.

Objective To compare the safety and efficacy of bupropion with methylphenidate in children and adolescents with attention-deficit/hyperactivity disorder (ADHD).

Methods In a 6-week randomized double-blind study, 44 patients with a DSM-IV-TR diagnosis of ADHD were randomly assigned to receive bupropion 100-150 mg/day (100 mg/day for <30 kg and 150 mg/day for >30 kg) or methylphenidate 20-30 mg/day. Symptoms were assessed using Teacher and Parent Attention-Deficit/Hyperactivity Disorder Rating Scale-IV (ADHD-RS-IV) at baseline and weeks 3 and 6.

Results Forty patients had at least one post-baseline measurement, and 38 patients completed the trial. No significant difference was found between the two groups on the Parent and Teacher ADHD-RS-IV scores ([F(1, 38) = 0.266, p = 0.609] and [F(1, 38) = 0.001, p = 0.972], respectively). By week 6, 18 patients (90%) in each group achieved response on the Parent scale (Fisher's exact test p-value = 1.0). With the Teacher ADHD-RS-IV used, eight (40%) patients in the bupropion group and 12 (60%) patients in the methylphenidate group achieved response by week 6 ((chi)2(1) = 1.600, p = 0.206). Headache was observed more frequently in the methylphenidate group. Frequency of other side effects was not significantly different between the two groups.

Conclusions Bupropion has a comparable safety and efficacy profile with methylphenidate in children and adolescents with ADHD.

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Int J Psychiatry Clin Pract. 2012;16:229-32.

THE EVALUATION OF CHILDREN WITH MONOSYMPTOMATIC NOCTURNAL ENURESIS FOR ATTENTION DEFICIT AND HYPERACTIVITY DISORDER.

Okur M, Ruzgar H, Erbey F, et al.

Objective. Monosymptomatic nocturnal enuresis (MNE) and attention deficit and hyperactivity disorder (ADHD) are multifactorial disorders and biological, social, and psychological factors may play significant roles in the development of both. Children with enuresis display a higher prevalence of ADHD compared to the normal population. This study aimed to evaluate the relationship between MNE and ADHD.

Methods. A total of 64 children between the ages of 6 and 13 years who were referred due to primary MNE, their parents, and 42 healthy control cases, were evaluated in terms of attention deficit and hyperactivity by a child psychiatrist using the DSM-IV-2000-TR diagnosic scale.

Results. Of the children with enuresis, 17 had predominantly inattentive type (26.6%), nine had predominantly hyperactive-impulsive type (14.1%), and eight had combined type (12.5%). In the control group, two cases had predominantly inattentive type (4.8%), two cases had predominantly hyperactive-impulsive type (4.8%), and one had combined type (2.4%).

Conclusions. The prevalence of ADHD is higher in children with MNE compared to the normal population. As attention deficit may also negatively effect the treatment of enuresis, children with MNE should be evaluated in terms of attention deficit and those with positive symptoms should be provided with psychosocial support.

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Int J Res Pharm Sci. 2012;3:282-86.

A STUDY OF EVALUATION OF SAFETY AND EFFICACY OF MEMOMET, A MULTI HERBAL FORMULATION (MEMOMET) IN THE TREATMENT OF BEHAVIOURAL DISORDER IN CHILDREN.

Dutta B, Barua TK, Ray J, et al.

This study shows the efficacy of Memomet in the treatment of ADHD in children. Total 86 patients were recruited in the study. There were 56 children in the treated group and 30 i n placebo treated group. The children were subjected to various test parameters like Yale's behavioural scale for children with ADHD, Conner's test and Malin's test. Both Memomet and Placebo was given at the dose of 1 tsf twice daily for 4 months. At the end of the study period both the groups were evaluated for response to treatment. It was observed that group treated with Memomet responded significantly compared to placebo.

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J Neuropsychiatry Clin Neurosci. 2012 Dec;24:95-101.

SYMPTOM PROFILE AND ETIOLOGY OF DELIRIUM IN A REFERRAL POPULATION IN NORTHERN INDIA: FACTOR ANALYSIS OF THE DRS-R98.

Mattoo SK, Grover S, Chakravarty K, et al.

Delirium is understudied in developing countries, where there tends to be a lower proportion of older persons and comorbid dementia. The authors assessed 100 consecutive cases of DSM-IV delirium (patients' mean age: 44.4 [standard deviation: 19.4] years; mean DRS-R98 score: 25.6 [3.6]) referred to an adult Consultation-Liaison Psychiatry service in Northern India. Disturbances of attention, orientation, visuospatial ability, and sleep disturbance were the most frequent symptoms, followed by language, thought-process abnormality, and motor agitation. A three-factor solution was identified, representing domains for cognition, higher-order thinking, and circadian rhythm/psychosis. These domains can guide studies addressing the relationship between symptom profile, therapeutic needs, and outcomes and are consistent with core domains previously identified in other countries.

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J Neuropsychiatry Clin Neurosci. 2012 Dec;24:111-14.

CAN COMPUTERIZED COGNITIVE TESTS ASSIST IN THE CLINICAL DIAGNOSIS OF ATTENTION-DEFICIT HYPERACTIVITY DISORDER?

Bloch Y, Fixman M, Maoz H, et al.

A group of 34 children and adolescents suspected of having attention-deficit hyperactivity disorder were referred for a computerized evaluation that included sustained attention, working memory, planning, and set-shifting. Although only sustained attention had reasonable specificity, all tests had questionable contribution to the diagnostic evaluation.

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J Abnorm Child Psychol. 2012 Jul;40:669-81.

CAN MOTIVATION NORMALIZE WORKING MEMORY AND TASK PERSISTENCE IN CHILDREN WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER? THE EFFECTS OF MONEY AND COMPUTER-GAMING.

Dovis S, van der Oord S, Wiers RW, et al.

Visual-spatial Working Memory (WM) is the most impaired executive function in children with Attention-Deficit/Hyperactivity Disorder (ADHD). Some suggest that deficits in executive functioning are caused by motivational deficits. However, there are no studies that investigate the effects of motivation on the visual-spatial WM of children with- and without ADHD. Studies examining this in executive functions other than WM, show inconsistent results. These inconsistencies may be related to differences in the reinforcement used. The effects of different reinforcers on WM performance were investigated in 30 children with ADHD and 31 non-ADHD controls. A visual-spatial WM task was administered in four reinforcement conditions: Feedback-only, 1 euro, 10 euros, and a computer-game version of the task. In the Feedback-only condition, children with ADHD performed worse on the WM measure than controls. Although incentives

significantly improved the WM performance of children with ADHD, even the strongest incentives (10 euros and Gaming) were unable to normalize their performance. Feedback-only provided sufficient reinforcement for controls to reach optimal performance, while children with ADHD required extra reinforcement. Only children with ADHD showed a decrease in performance over time. Importantly, the strongest incentives (10 euros and Gaming) normalized persistence of performance in these children, whereas 1 euro had no such effect. Both executive and motivational deficits give rise to visual-spatial WM deficits in ADHD. Problems with task-persistence in ADHD result from motivational deficits. In ADHD-reinforcement studies and clinical practice (e.g., assessment), reinforcement intensity can be a confounding factor and should be taken into account. Gaming can be a cost-effective way to maximize performance in ADHD.

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J Abnorm Child Psychol. 2012 Aug;40:987-98.

IS THE POSITIVE ILLUSORY BIAS ILLUSORY? EXAMINING DISCREPANT SELF-PERCEPTIONS OF COMPETENCE IN GIRLS WITH ADHD.

Swanson EN, Owens EB, Hinshaw SP.

It has been claimed that excessively positive self-perceptions of competence are a key risk factor for concurrent and subsequent impairments in youth with attention-deficit/ hyperactivity disorder (ADHD). We examined whether girls with ADHD demonstrate positive illusory self-perceptions in scholastic competence, social acceptance, and behavioral conduct domains. We then tested, across a five-year longitudinal span, whether (a) such self-perceptions versus (b) the constituent informant ratings or test scores were more strongly predictive of adolescent impairment and positive adjustment. Participants included an ethnically diverse sample of 140 girls with ADHD and 88 comparison girls, aged 6–12 at baseline (M = 9.0, SD = 1.7). Girls with ADHD rated themselves as more positive than indicated by external ratings, but these self-reports were still in a negative direction (comparison girls rated themselves as less positive than these indicators). ADHD subtypes were not related to discrepancy scores. Higher rates of depression symptoms were associated with attenuated discrepancy scores. Crucially, measures of actual competence were more strongly associated with adolescent impairment and positive adjustment than were "illusory" self-perceptions for girls with ADHD. Our findings challenge the view that, at least in girls with ADHD, overly positive and "illusory" appraisals of competence are strongly associated with future impairment and adjustment. The key psychometric point is that, in difference or discrepancy scores, the individual components of such scores should be separately examined.

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J Abnorm Child Psychol. 2012 Jul;40:683-97.

VALIDITY OF THE SLUGGISH COGNITIVE TEMPO, INATTENTION, AND HYPERACTIVITY SYMPTOM DIMENSIONS: NEUROPSYCHOLOGICAL AND PSYCHOSOCIAL CORRELATES.

Bauermeister JJ, Barkley RA, Bauermeister JA, et al.

This study examined the latent structure and validity of inattention, hyperactivity-impulsivity, and sluggish cognitive tempo (SCT) symptomatology. We evaluated mother and teacher ratings of ADHD and SCT symptoms in 140 Puerto Rican children (55.7% males), ages 6 to 11 years, via factor and regression analyses. A three-factor model (inattention, hyperactivity-impulsivity, and SCT) provided the best fit for both sets of ratings. Inattention was the strongest correlate of lower scores on neuropsychological, achievement, and psychosocial measures. Externalizing problems were most strongly associated with hyperactivity-impulsivity, and internalizing problems were most strongly associated with parent-rated SCT and teacher-rated Inattention. SCT was not associated with executive function but was negatively associated with math. Inattention accounted for a disproportionate amount of ADHD-related impairment, which may explain the restricted discriminant validity of DSM-IV types. The distinct factors of hyperactivity-impulsivity and SCT had unique associations with impairing comorbidities and are roughly equivalent in predicting external correlates of ADHD-related impairment.

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J Abnorm Child Psychol. 2012 Aug;40:999-1011.

UNDERSTANDING PHONOLOGICAL MEMORY DEFICITS IN BOYS WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER (ADHD): DISSOCIATION OF SHORT-TERM STORAGE AND ARTICULATORY REHEARSAL PROCESSES.

Bolden J, Rapport MD, Raiker JS, et al.

The current study dissociated and examined the two primary components of the phonological working memory subsystem—the short-term store and articulatory rehearsal mechanism—in boys with ADHD (n = 18) relative to typically developing boys (n = 15). Word lists of increasing length (2, 4, and 6 words per trial) were presented to and recalled by children following a brief (3 s) interval to assess their phonological short-term storage capacity. Children's ability to utilize the articulatory rehearsal mechanism to actively maintain information in the phonological short-term store was assessed using word lists at their established memory span but with extended rehearsal times (12 s and 21 s delays). Results indicate that both phonological short-term storage capacity and articulatory rehearsal are impaired or underdeveloped to a significant extent in boys with ADHD relative to typically developing boys, even after controlling for age, SES, IQ, and reading speed. Larger magnitude deficits, however, were apparent in short-term storage capacity (ES = 1.15 to 1.98) relative to articulatory rehearsal (ES = 0.47 to 1.02). These findings are consistent with previous reports of deficient phonological short-term memory in boys with ADHD, and suggest that future attempts to develop remedial cognitive interventions for children with ADHD will need to include active components that require children to hold increasingly more information over longer time intervals.

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J Abnorm Child Psychol. 2012 Aug;40:1013-26.

PEER REJECTION AND FRIENDSHIPS IN CHILDREN WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER: CONTRIBUTIONS TO LONG-TERM OUTCOMES.

Mrug S, Molina BSG, Hoza B, et al.

Even after evidence-based treatment, Attention-Deficit/Hyperactivity Disorder (ADHD) is associated with poor long-term outcomes. These outcomes may be partly explained by difficulties in peer functioning, which are common among children with ADHD and which do not respond optimally to standard ADHD treatments. We examined whether peer rejection and lack of dyadic friendships experienced by children with ADHD after treatment contribute to long-term emotional and behavioral problems and global impairment, and whether having a reciprocal friend buffers the negative effects of peer rejection. Children with Combined type ADHD (N = 300) enrolled in the Multimodal Treatment Study of Children with ADHD (MTA) were followed for 8 years. Peer rejection and dyadic friendships were measured with sociometric assessments after the active treatment period (14 or 24 months after baseline; M ages 9.7 and 10.5 years, respectively). Outcomes included delinquency, depression, anxiety, substance use, and general impairment at 6 and 8 years after baseline (Mean ages 14.9 and 16.8 years, respectively). With inclusion of key covariates, including demographics, symptoms of ADHD, ODD, and CD, and level of the outcome variable at 24 months, peer rejection predicted cigarette smoking, delinquency, anxiety, and global impairment at 6 years and global impairment at 8 years after baseline. Having a reciprocal friend was not, however, uniquely predictive of any outcomes and did not reduce the negative effects of peer rejection. Evaluating and addressing peer rejection in treatment planning may be necessary to improve long-term outcomes in children with ADHD.

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J Abnorm Child Psychol. 2012 Jul;40:657-68.

CHILDHOOD EXECUTIVE FUNCTION CONTINUES TO PREDICT OUTCOMES IN YOUNG ADULT FEMALES WITH AND WITHOUT CHILDHOOD-DIAGNOSED ADHD.

Miller M, Nevado-Montenegro AJ, Hinshaw SP.

We prospectively followed an ethnically and socioeconomically diverse sample of preadolescent girls with ADHD (n = 140) and matched comparison girls (n = 88) over a period of 10 years, from middle childhood through late adolescence/young adulthood. Our aim was to examine the ability of childhood measures of executive function (EF) to predict functional outcomes at follow-up. Measures of EF comprised the childhood predictors, with academic, socioemotional, occupational, and global functioning serving as young

adult criterion measures. Results indicated that childhood EF—particularly measures of global EF and working memory—predicted academic and occupational functioning across our entire sample (independent of diagnostic group status), but diagnostic status (ADHD versus comparison) moderated the association between (a) working memory and reading achievement and (b) a global EF measure and suspensions/expulsions. That is, in the ADHD group, low working memory predicted poor reading scores and impaired global EF predicted higher suspensions/expulsions, but this was not the case in the comparison group. Overall, these results extend previous findings of associations between EF and adolescent outcomes in girls with and without ADHD into young adulthood. Findings continue to suggest the importance of assessing and developing interventions that target EF impairments early in life in order to prevent long-term difficulties across a range of important functional domains.

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J Abnorm Child Psychol. 2012 Jul;40:699-713.

OBJECTIVELY-MEASURED IMPULSIVITY AND ATTENTION-DEFICIT/HYPERACTIVITY DISORDER (ADHD): TESTING COMPETING PREDICTIONS FROM THE WORKING MEMORY AND BEHAVIORAL INHIBITION MODELS OF ADHD.

Raiker JS, Rapport MD, Kofler MJ, et al.

Impulsivity is a hallmark of two of the three DSM-IV ADHD subtypes and is associated with myriad adverse outcomes. Limited research, however, is available concerning the mechanisms and processes that contribute to impulsive responding by children with ADHD. The current study tested predictions from two competing models of ADHD—working memory (WM) and behavioral inhibition (BI)—to examine the extent to which ADHD-related impulsive responding was attributable to model-specific mechanisms and processes. Children with ADHD (n = 21) and typically developing children (n = 20) completed laboratory tasks that provided WM (domain-general central executive [CE], phonological/visuospatial storage/rehearsal) and BI indices (stop-signal reaction time [SSRT], stop-signal delay, mean reaction time). These indices were examined as potential mediators of ADHD-related impulsive responding on two objective and diverse laboratory tasks used commonly to assess impulsive responding (CPT: continuous performance test; VMTS: visual match-to-sample). Bias-corrected, boot-strapped mediation analyses revealed that CE processes significantly attenuated between-group impulsivity differences, such that the initial large-magnitude impulsivity differences were no longer significant on either task after accounting for ADHD-related CE deficits. In contrast, SSRT partially mediated ADHD-related impulsive responding on the CPT but not VMTS. This partial attenuation was no longer significant after accounting for shared variance between CE and SSRT; CE continued to attenuate the ADHD-impulsivity relationship after accounting for SSRT. These findings add to the growing literature implicating CE deficits in core ADHD behavioral and functional impairments, and suggest that cognitive interventions targeting CE rather than storage/rehearsal or BI processes may hold greater promise for alleviating ADHD-related impairments.

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J Affective Disord. 2012.

ATTENTION DEFICIT HYPERACTIVITY DISORDER CHARACTERISTICS: II. CLINICAL CORRELATES OF IRRITABLE MOOD.

Ambrosini PJ, Bennett DS, Elia J.

Background: This study describes the relationship of irritable mood (IRR) with affective disorders in youths with attention deficit hyperactivity disorder (ADHD).

Methods: Five hundred ADHD subjects were assessed with the childhood version of the Schedule for Affective Disorder & Schizophrenia. Subjects were in a genetic ADHD protocol and limited to those of Caucasian/European descent.

Results: The most prevalent concurrent diagnoses were oppositional defiant disorder (ODD) (43.6%), minor depression/dysthymic disorder (MDDD) (18.8%), and generalized anxiety (13.2%)/overanxious disorder (12.4%). IRR subjects (21.0%) compared to the non-IRR (NIRR) group had higher rates of all affective disorders (76.2% vs. 9.6%) and ODD (83.8% vs. 32.9%) but lower rates of hyperactive ADHD (1.9% vs. 8.9%). Among those without comorbidities, 98.3% were NIRR. Logistic regression found IRR mood significantly associated with major depressive disorder (odds ratio [OR]: 33.4), MDDD (OR: 11.2), ODD (OR: 11.6), and combined ADHD (OR: 1.7) but not with anxiety disorders. Among symptoms, it

associated IRR mood with a pattern of dysthymic and ODD symptoms but with fewer separation anxiety symptoms. Diagnostic and symptomatic parameters were unaffected by demographic variables.
Limitations: Potential confounders influencing these results include patient recruitment from only one clinical service; a cohort specific sample effect because some presumed affective disorders and non-Caucasians were excluded; and the young mean age (10.2 years) limiting comorbid patterns.
Conclusions: The prominence of an MDDD pattern suggests this IRR group is appropriate in the DSM V's proposed chronic depressive disorder, possibly with or without temper dysregulation. A new diagnosis of disruptive mood dysregulation disorder may be unwarranted.

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J Autism Dev Disord. 2012;1-11.
LEARNING CURVE ANALYSES IN NEURODEVELOPMENTAL DISORDERS: ARE CHILDREN WITH AUTISM SPECTRUM DISORDER TRULY VISUAL LEARNERS?
Erdodi L, Lajiness-O'Neill R, Schmitt TA.
Visual and auditory verbal learning using a selective reminding format was studied in a mixed clinical sample of children with autism spectrum disorder (ASD) (n=42), attention-deficit hyperactivity disorder (n=83), velocardiofacial syndrome (n=17) and neurotypicals (n=38) using the Test of Memory and Learning to (1) more thoroughly characterize and examine the integrity of learning and memory processes, (2) to better understand the mechanisms of learning impairment, and (3) to inform instructional practices in ASD. Contrary to expectations, children with ASD demonstrated a relative weakness in the rate of acquisition of visual in contrast to verbal learning compared to neurotypicals. They also showed a complex pattern of consolidation. Overall, between-group differences were more likely to emerge during the visual learning task, suggesting that it may be more sensitive for detecting neurodevelopmental differences. The heuristic value of assessing memory and learning across multiple trials and comparing performance during immediate and delayed recall is discussed.

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J Child Adolesc Psychopharmacol. 2012 Jun;22:456-57.
A CASE OF EXCESSIVE WEIGHT GAIN WITH GUANFACINE EXTENDED RELEASE: 9.53 KG IN 4 WEEKS.
Khan MA, Jain G, Soltys SM, et al.
Presents a case report of a 7-year-and-5-month-old Caucasian boy, had the diagnosis of Asperger's disorder and ADHD per Diagnostic and Statistical Manual of Mental Disorders, 4th edition. He was referred to the clinic due to poorly controlled ADHD symptoms, despite treatment with mixed amphetamine salts, 10 mg three times a day, for over 9 months. His weight, height, and body mass index (BMI) on presentation were 32.7 kg, 128.3 cm, and 19.9, respectively. He had history of failed trials with methylphenidate. The mixed amphetamine salts were discontinued and he was placed on GXR 1mg in the morning. He experienced somnolence and fatigue during day time but it gradually improved. After 1 week, he weighed 33.6 kg; GXR was increased to 2 mg/day. Three weeks later, his ADHD symptoms improved significantly. During this period, his routine of physical activities, television watching, and eating habits remained unchanged. He was not on any other medications. GXR was decreased to 1mg/day due to concerning weight gain. mL). With the decrease in GXR dose he gained 1.4 more kilograms in the next 2 weeks but the ADHD symptoms worsened. He was switched to atomoxetine 18 mg/day twice daily. Eight weeks after GXR discontinuation, he had lost 1.8 kg and his BMI decreased to 23.6.

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Journal of Child Psychology and Psychiatry. 2012 Jul;53:782-89.
TIME-OF-DAY EFFECTS IN AROUSAL: DISRUPTED DIURNAL CORTISOL PROFILES IN CHILDREN WITH ADHD.
Imeraj L, Antrop I, Roeyers H, et al.
Background: Fluctuations in attention-deficit hyperactivity disorder (ADHD) symptoms related to regulatory deficits in arousal states are themselves characterized by circadian rhythms. Although cortisol is an

important circadian arousal-related marker, studies focusing on across-the-day cortisol variations in ADHD are scarce. There is no study with multiple measurements to take into account interday and intraday variability.
Methods: Salivary cortisol was sampled five times a day (awakening, 30 min after awakening, noon, 4 p.m., 8 p.m.) across five consecutive days in 33 children with ADHD (22 with and 11 without oppositional defiant disorder; ODD) and 33 class- and sex-matched controls (aged 6–12). The cortisol awakening response (increase from awakening to 30 min after awakening) and the diurnal cortisol profile (across-the-day variations) were compared for ADHD with ODD (ADHD + ODD) and without ODD (ADHD) subgroups and the control group.
Results: The cortisol awakening response was not significantly different between groups. However, longitudinal analyses to evaluate cortisol profiles across the day revealed a significant Group × Time effect ($p<.001$). More specifically, compared to each other, the ADHD subgroup showed a flatter slope with relative morning hypo-arousal and evening hyperarousal, whereas the ADHD + ODD subgroup showed a steeper slope with relative morning hyperarousal and evening hypo-arousal ($p<.001$).
Conclusions: Findings support time-related arousal disruptions in children with ADHD associated with the presence or absence of ODD comorbidity. We recommend research on cortisol in larger samples for a better understanding of arousal mechanisms involved in ADHD not only with and without ODD but also with other comorbidities which may have implications for timing of arousal-based treatments.

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Journal of Child Psychology and Psychiatry. 2012 Aug;53:864-73.
AETIOLOGY FOR THE COVARIATION BETWEEN COMBINED TYPE ADHD AND READING DIFFICULTIES IN A FAMILY STUDY: THE ROLE OF IQ.
Cheung CHM, Wood AC, Paloyelis Y, et al.
Background: Twin studies using both clinical and population-based samples suggest that the frequent co-occurrence of attention deficit hyperactivity disorder (ADHD) and reading ability/disability (RD) is largely driven by shared genetic influences. While both disorders are associated with lower IQ, recent twin data suggest that the shared genetic variability between reading difficulties and ADHD inattention symptoms is largely independent from genetic influences contributing to general cognitive ability. The current study aimed to extend the previous findings that were based on rating scale measures in a population sample by examining the generalisability of the findings to a clinical population, and by measuring reading difficulties both with a rating scale and with an objective task. This study investigated the familial relationships between ADHD, reading difficulties and IQ in a sample of individuals diagnosed with ADHD combined type, their siblings and control sibling pairs.
Methods: Multivariate familial models were run on data from 1,789 individuals at ages 6–19. Reading difficulties were measured with both rating scale and an objective task. IQ was obtained using the Wechsler Intelligence Scales (WISC–III/WAIS–III).
Results: Significant phenotypic (.2–.4) and familial (.3–.5) correlations were observed among ADHD, reading difficulties and IQ. Yet, 53%–72% of the overlapping familial influences between ADHD and reading difficulties were not shared with IQ.
Conclusions: Our finding that familial influences shared with general cognitive ability, although present, do not account for the majority of the overlapping familial influences on ADHD and reading difficulties extends previous findings from a population-based study to a clinically ascertained sample with combined type ADHD.

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Journal of Child Psychology and Psychiatry. 2012 Aug;53:892-902.
LPHN3 AND ATTENTION-DEFICIT/HYPERACTIVITY DISORDER: INTERACTION WITH MATERNAL STRESS DURING PREGNANCY.
Choudhry Z, Sengupta SM, Grizenko N, et al.
Background: Attention-deficit/hyperactivity disorder (ADHD) is a heterogeneous behavioral disorder, complex both in etiology and clinical expression. Both genetic and environmental factors have been

implicated, and it has been suggested that gene-environment interactions may play a pivotal role in the disorder. Recently, a significant association was reported between ADHD and LPHN3 (which codes for latrophilin 3), and replicated in independent samples.
Methods: We have examined the association between tag single nucleotide polymorphisms (SNPs) in LPHN3 within the region previously implicated in ADHD. Family based association tests (FBAT) were conducted (n = 380 families) with the categorical diagnosis of ADHD, behavioral and cognitive phenotypes related to ADHD, and response to treatment (given a fixed dose of methylphenidate, 0.5 mg/day). Stratified FBAT analyses, based on maternal smoking and stress during pregnancy, was conducted.
Results: Whereas limited association was observed in the total sample, highly significant interaction between four LPHN3 tag SNPs (rs6551665, rs1947274, rs6858066, rs2345039) and maternal stress during pregnancy was noted. Analysis conducted in the sub-group of mothers exposed to minimal stress during pregnancy showed significant associations with ADHD, behavioral and cognitive dimensions related to ADHD, as well as treatment response. Although extensive association was observed with the candidate SNPs, the findings are partially inconsistent with previously published results with the opposite alleles over-transmitted in these studies.
Conclusions: These results provide evidence for the interaction between a genetic and environmental factor independently shown to be associated with ADHD. If confirmed in independent large studies, they may present a step forward in unraveling the complex etiology of ADHD.

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J Consult Clin Psychol. 2012 Aug;80:611-23.

A FAMILY–SCHOOL INTERVENTION FOR CHILDREN WITH ADHD: RESULTS OF A RANDOMIZED CLINICAL TRIAL.

Power TJ, Mautone JA, Soffer SL, et al.

Objective: Accumulating evidence highlights the importance of using psychosocial approaches to intervention for children with attention-deficit/hyperactivity disorder (ADHD) that target the family and school, as well as the intersection of family and school. This study evaluated the effectiveness of a family–school intervention, Family–School Success (FSS), designed to improve the family and educational functioning of students in Grades 2–6 who meet criteria for ADHD combined and inattentive types. Key components of FSS were conjoint behavioral consultation, daily report cards, and behavioral homework interventions.
Method: FSS was provided over 12 weekly sessions, which included 6 group sessions, 4 individualized family sessions, and 2 school-based consultations. Participating families were given the choice of placing their children on medication; 43% of children were on medication at the time of random assignment. Children (n=199) were randomly assigned to FSS or a comparison group controlling for non-specific treatment effects (Coping With ADHD Through Relationships and Education [CARE]). Outcomes were assessed at post-intervention and 3-month follow-up. The analyses controlled for child medication status.
Results: FSS had a significant effect on the quality of the family–school relationship, homework performance, and parenting behavior.
Conclusions: The superiority of FSS was demonstrated even though about 40% of the participants in FSS and CARE were on an optimal dose of medication and there were significant time effects on each measure. This relatively brief intervention produced effect sizes comparable to those of the more intensive Multimodal Treatment Study of Children With ADHD (MTA) behavioral intervention.

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Journal of Educational Psychology. 2012 Aug;104:529-40.

"THE SNAKE RAISED ITS HEAD": CONTENT NOVELTY ALTERS THE READING PERFORMANCE OF STUDENTS AT RISK FOR READING DISABILITIES AND ADHD.

Beike SM, Zentall SS.

The purpose of this study was to assess the effects of story novelty (active verbs, less familiar characters, vivid adjectives, and surprising story endings) on the reading comprehension of 48 seven- to 11-year-old boys without clinical diagnoses of learning disabilities. The optimal stimulation theory provided the basis of the study, predicting differential response to novelty by 3 groups of equivalent-IQ boys, who were at risk for

reading disabilities (RD; n = 16), at risk for attention-deficit/hyperactivity disorder (ADHD; n = 16), and typically developing (n = 16). Across conditions, the RD group performed worse than typical students in the comprehension of individually graded passages and worse than the ADHD group in causality comprehension. More important, the predicted interaction in support of theory documented better reading performance in the high- than the low-novelty condition for both at-risk groups and, specifically, in causality and inferential comprehension. In other words, it was the low-novelty reading condition that exacerbated group differences in reading comprehension. The novelty-based gains were interpreted as byproducts of increased student activation, facilitating attention for the at-risk ADHD group, who have a greater need for stimulation (novelty), and for students at risk for RD to combat fatigue associated with skill deficits.

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J Med Syst. 2012;36:1335-43.

DESIGNING A DECISION SUPPORT SYSTEM FOR DISTINGUISHING ADHD FROM SIMILAR CHILDREN BEHAVIORAL DISORDERS.

Delavarian M, Towhidkhah F, Dibajnia P, et al.

In this study, a decision support system was designed to distinguish children with ADHD from other similar children behavioral disorders such as depression, anxiety, comorbid depression and anxiety and conduct disorder based on the signs and symptoms. Accuracy of classifying with Radial basis function and multilayer neural networks were compared. Finally, the average accuracy of the networks in classification reached to 95.50% and 96.62% by multilayer and radial basis function networks respectively. Our results indicate that a decision support system, especially RBF, may be a good preliminary assistant for psychiatrists in diagnosing high risk behavioral disorders of children.

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J Neurol. 2012;1-10.

HIGH-THROUGHPUT CLASSIFICATION OF CLINICAL POPULATIONS FROM NATURAL VIEWING EYE MOVEMENTS.

Tseng PH, Cameron IGM, Pari G, et al.

Many high-prevalence neurological disorders involve dysfunctions of oculomotor control and attention, including attention deficit hyperactivity disorder (ADHD), fetal alcohol spectrum disorder (FASD), and Parkinson's disease (PD). Previous studies have examined these deficits with clinical neurological evaluation, structured behavioral tasks, and neuroimaging. Yet, time and monetary costs prevent deploying these evaluations to large at-risk populations, which is critically important for earlier detection and better treatment. We devised a high-throughput, low-cost method where participants simply watched television while we recorded their eye movements. We combined eye-tracking data from patients and controls with a computational model of visual attention to extract 224 quantitative features. Using machine learning in a workflow inspired by microarray analysis, we identified critical features that differentiate patients from control subjects. With eye movement traces recorded from only 15 min of videos, we classified PD versus age-matched controls with 89.6 % accuracy (chance 63.2 %), and ADHD versus FASD versus control children with 77.3 % accuracy (chance 40.4 %). Our technique provides new quantitative insights into which aspects of attention and gaze control are affected by specific disorders. There is considerable promise in using this approach as a potential screening tool that is easily deployed, low-cost, and high-throughput for clinical disorders, especially in young children and elderly populations who may be less compliant to traditional evaluation tests.

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J Orthomol Med. 2012;27:51-52.

THE VITAMIN TREATMENT OF HYPERACTIVITY: A SAFE AND ETHICAL WAY IN WHICH TO TREAT OUR CHILDREN.

Prousky JE.

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J Pediatr. 2012.

DO STIMULANTS REDUCE THE RISK FOR CIGARETTE SMOKING IN YOUTH WITH ATTENTION-DEFICIT HYPERACTIVITY DISORDER? A PROSPECTIVE, LONG-TERM, OPEN-LABEL STUDY OF EXTENDED-RELEASE METHYLPHENIDATE.

Hammerness P, Joshi G, Doyle R, et al.

Objective: Although attention-deficit hyperactivity disorder (ADHD) is a well-known risk factor for cigarette smoking, prospective studies aimed at reducing smoking risk in this population are critically needed.

Study design: This was a 2-year, prospective, open-label clinical trial of extended-release methylphenidate for smoking prevention in adolescents with ADHD (n = 154). Smoking outcomes were assessed with the Fagerstrom Tolerance Questionnaire. Comparisons were made using data from a historical, naturalistic sample of ADHD (n = 103) and non-ADHD comparators (n = 188) of similar age and sex assessed with the same assessment battery as that used in subjects participating in the clinical trial.

Results: The smoking rate at endpoint (mean, 10 months of methylphenidate treatment) was low in the clinical trial subjects and not significantly different from that in the non-ADHD comparators or the ADHD comparators receiving stimulants naturalistically (7.1% vs 8.0% vs 10.9%; P > .20). In contrast, the smoking rate was significantly lower in the clinical trial subjects than in the naturalistic sample of ADHD comparators who were not receiving stimulant treatment (7.1% vs 19.6%; P = .009 [not significant], adjusting for comorbid conduct disorder and alcohol and drug abuse).

Conclusion: Although considered preliminary until replicated in future randomized clinical trials, the findings from this single-site, open-label study suggest that stimulant treatment may contribute to a decreased risk for smoking in adolescents with ADHD. If confirmed, this finding would have significant clinical and public health impacts.

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J Psychopathol Behav Assess. 2012;1-10.

AN INTENSIVE SUMMER TREATMENT PROGRAM FOR ADHD REDUCES PARENT-ADOLESCENT CONFLICT.

Sibley MH, Ross JM, Gnagy EM, et al.

There are currently almost no treatment efforts to reduce parent-adolescent conflict in adolescents with ADHD. As such, this study investigated the effect of an intensive Summer Treatment Program for Adolescents with ADHD (STP-A) on parent-adolescent conflict. Twenty adolescents and their parents completed the 8 week behavioral treatment program, which included 320 hours of adolescent-directed treatment, 15 hours of parent behavior management training, and daily feedback from staff on parent implementation of a home-based behavioral contract. Results indicated that 70-85 % of adolescents who attended the STP-A demonstrated reliable improvement in parent-adolescent conflict from baseline to post-treatment. Treatment response was associated with higher levels of conflict at baseline, but not adolescent ODD severity or parent ADHD severity. Several patterns of treatment non-response were detected through visual examination of weekly conflict scores during the STP-A. Discussion suggests that intensive, parent-involved treatment programs may be necessary to improve home-conflict in adolescents with ADHD.

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Nervenheilkunde. 2012;31:536-42.

ATTENTION-DEFICIT/HYPERACTIVITY DISORDER ACROSS THE LIFE SPAN.

Klein C.

Attention-deficit/hyperacitivity disorder (ADHD) belongs with a prevalence estimate of about 5.3% to the most common psychiatric disorders of childhood and adolescence. ADHD is a developmental disorder that interacts in an unfavourable manner with the typical course of development. This implies that, in addition to the core symptoms of inattention, impulsivity and hyperactivity, secondary symptoms and deficits in academic and social functioning that are acquired during the course of development must be considered. Furthermore, comorbid disorders such as conduct disorder, oppositional-defiant disorder or anxiety disorders need to be considered here. The aetiology of ADHD is presumably rather complex, with genetic factors, gene-environment interactions and gene-environment correlations being relevant. The treatment of ADHD involves pharmacologically the administration of psycho-stimulants, and psychologically or psycho-

therapeutically behavioural therapy, specific training procedures and, more recently, neurofeedback techniques.

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Neurologia. 2012.

EVALUATING EXECUTIVE FUNCTION IN SCHOOLCHILDREN WITH SYMPTOMS OF ATTENTION DEFICIT HYPERACTIVITY DISORDER.

Velez-van-Meerbeke A, Zamora IP, Guzman G, et al.

Objective: To identify impairment of executive functions (EF) in children with attention deficit hyperactivity disorder (ADHD).

Subjects and methods: A case-control study was performed on a sample of schoolchildren with low socioeconomic levels in Bogota, Colombia. ADHD was diagnosed using the DSM IV checklist and the Behavior Assessment System for Children scale. Children with cognitive deficits were excluded. We evaluated scores from six measurements of executive function (EF). We conducted a bivariate statistical analysis to compare the variables, a multivariate study controlled by sex and age, and a logistic regression analysis.

Results: The study sample included 119 children with ADHD and 85 controls, all aged between 6 and 12 years. Controlling by sex, age, and type of school showed that EF measurements in children with ADHD were significantly more impaired than in controls, especially for measurements of verbal and graphic fluency, Rey-Osterrieth Complex Figure, and cognitive flexibility. Comparison of ADHD subgroups showed that results in children with multiple deficits were similar to those in the global ADHD group. Graphic fluency impairment was the sole impairment in cases with only attention deficit or only hyperactivity-impulsivity manifestations.

Conclusions: EF measures in children with ADHD revealed more problems, particularly those having to do within planning, inhibition, working memory and cognitive control. Age and sex may affect the degree of EF impairment.

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No To Hattatsu. 2012;44:289-94.

THE EFFECT OF PARENT TRAINING PROGRAM ON CHILDREN WITH ATTENTION DEFICIT/HYPERACTIVITY DISORDERS AND/OR PERVASIVE DEVELOPMENTAL DISORDERS.

Motoyama K, Matsuzaka T, Nagaoka T, et al.

Mothers of 18 children with attention deficit/hyperactivity disorders (AD/HD) and 6 with pervasive developmental disorders (PDD) ~underwent a parent training (PT) program. After the program, the Beck Depression Inventory- II (BDI-II) score, which indicates parenting ~stress, significantly decreased from 15 to 8 (p=0.036). A total of 22 mothers had increased parenting self-esteem, and better parent-child ~relationships were noted in these cases. An analysis of children's behavior by using Achenbach's Child Behavior Checklist showed that ~introversion tendency, physical failure, aggressive behavior, and extroversion score improved significantly after PT (p<0.05). After PT, ~out-of-control behaviors improved in 19 children and continued in 5. We conclude that PT for mothers of children with AD/HD and/or ~high-functioning PDD is effective in improving both the parenting skills of mothers and adaptive behaviors of children.

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No To Hattatsu. 2012;44:320-26.

EFFECTIVENESS OF SOCIAL SKILLS TRAINING FOR CHILDREN WITH DEVELOPMENTAL DISORDERS: BEHAVIORAL ANALYSIS USING A TWO-DIMENSIONAL MOTION CAPTURE SYSTEM.

Sakuma R, Gunji A, Goto T, et al.

The current study sought to develop a new behavioral analysis methods to evaluate the effects of social skills training (SST). SST is known to be an effective method to improve the social skills of children with

behavioral problems. However, current evaluation methods involve behavioral rating scales that are heavily dependent on evaluators' particular experiences they have had. To quantitatively examine the behavioral effects of SST, we examined subjects' head-movements related to social behavior, using a two-dimensional motion capture system (Kissei Comtec, Japan). Four children (three male, one female, 7-8 years of age) with pervasive developmental disorder (PDD) or attention deficit/hyperactivity disorder (AD/HD) participated in 16 sessions of SST. Before and after SST, head-coordinates on a two-dimensional plane were calculated using their behavior during a pair task, measured by four digital cameras. After SST, the number of communication behaviors was increased compared to before SST. In addition, children looked longer at another child within 30 degrees of the central visual field. Time-series analysis of the visual field during the detection of another child revealed significant auto-correlation from about - 1.12 second, before to the beginning of communication behavior ($p<0.05$). The results suggested mat our method can provide a quantitative index of characteristics related to skilled social behaviors. We conclude mat a two-dimensional motion capture system would be useful for visualization of the interventional effects of SST, which would supplement assessments by the conventional observational strategies.

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Pediatr Neurol. 2012;47:177-85.

TRANSCRANIAL MAGNETIC STIMULATION MEASURES IN ATTENTION-DEFICIT/ HYPERACTIVITY DISORDER.

Wu SW, Gilbert DL, Shahana N, et al.

Children affected by attention-deficit/hyperactivity disorder demonstrate diminished intrahemispheric inhibition (short interval cortical inhibition), as measured by transcranial magnetic stimulation. This study determined whether interhemispheric inhibition (ipsilateral silent period latency) correlates with clinical behavioral rating and motor control deficits of affected children. In 114 right-handed children (aged 8-12 years; age/sex-matched; 50 affected, 64 controls), we performed comprehensive assessments of behavior, motor skills, and cognition. Transcranial magnetic stimulation reliably elicited ipsilateral silent periods in 54 children (23 affected); all were on average older than those with unobtainable measures. Mean ipsilateral silent period latency was 5 milliseconds longer in the affected group ($P = 0.007$). Longer latencies correlated with more severe behavioral symptom scores ($r = 0.38$, $P = 0.007$), particularly hyperactivity ($r=0.39$, $P=0.006$), and with worse motor ratings on the Physical and Neurological Examination for Soft Signs ($r=0.27$, $P=0.05$). Longer latency also correlated with short interval cortical inhibition ($r=0.36$, $P=0.008$). Longer ipsilateral silent period latencies suggest interhemispheric inhibitory signaling is slower in affected children. The deficit in this inhibitory measure may underlie developmental, behavioral, and motor impairments in children with attention-deficit/hyperactivity disorder.

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Pediatr Int. 2012;54:546-49.

ATOMOXETINE IMPROVES COMMUNICATION IN A GIRL WITH SEMANTIC-PRAGMATIC DISORDER.

Inoko K, Kodaira K, Osawa M.

This report describes the case of an ADHD girl (hereafter referred to as K) with semantic-pragmatic disorder, she was treated with atomoxetine. K was a 9-year-old girl. She had difficulty understanding words or sentences, finding words, and producing sentences. K also displayed symptoms of severe inattentiveness. K was diagnosed with DSM-IV-defined1 ADHD, predominantly the inattentive type. Her communication impairment was considered symptomatic of semantic-pragmatic disorder. K was started on atomoxetine, the dose was increased to 50 mg/day (dosage based on weight: 1.8 mg/kg). Her communication activities were improved a few weeks after atomoxetine 50 mg/day was administered. She was unable to organize information pertaining to words, and so could not use words in expressive language. These problems were mitigated through the administration of atomoxetine. Further prospective studies are needed to better understand the therapeutic effects of atomoxetine in patients with semantic-pragmatic disorder.

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Prim Care Companion J Clin Psych. 2012;14.

A QUICK TEST OF COGNITIVE SPEED FOR COMPARING PROCESSING SPEED TO DIFFERENTIATE ADULT PSYCHIATRIC REFERRALS WITH AND WITHOUT ATTENTION-DEFICIT/HYPERACTIVITY DISORDERS.

Wiig EH, Nielsen NP.

Objective: This retrospective study used A Quick Test of Cognitive Speed (AQT) to compare processing speed and efficiency measures by adults with attention-deficit/hyperactivity disorder (ADHD) or non-ADHD psychiatric disorders and healthy controls.

Method: Color, form, and color-form combination naming tests were administered to 104 adults, ages 17-55 years, referred for psychiatric evaluation of possible ADHD. Thirty healthy adults were controls. Psychiatric intake procedures identified 64 adults with ADHD (ICD-10 and DSM-IV criteria) and 40 with mild psychiatric disorders without ADHD. The study was conducted from 2008 through 2010.

Results: At intake, color, form, and color-form combination naming times (seconds) were longer and overhead [color-form combination - (color + form)] was larger for patients with ADHD than for non-ADHD patients and controls. In the ADHD group, color and form measures were in the normal range. Color-form combination was in the slower-than-normal speed (60-70 seconds) and overhead, a processing-efficiency measure, in the atypical range (> 10 seconds). In the non-ADHD patient and control groups, all AQT measures were in the normal range. Analysis of variance with post hoc analysis of log-normal values for color, form, and color-form combination and time for overhead indicated significant (Bonferroni P <.01) mean differences between the ADHD and other groups, but not between the non-ADHD and control groups. When using fail criteria for either color-form combination or overhead, the sensitivity for the ADHD group was 89%.

Conclusions: Results support AQT as a possible complement to psychiatric intake procedures to differentiate adults with ADHD from those with mild psychiatric disorders, and they suggest that a controlled prospective study might be productive.

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Psychiatric Genetics 2012;22:202-205.

ATTENTION-DEFICIT-HYPERACTIVITY DISORDER AND BINGE EATING DISORDER IN A PATIENT WITH 2Q21.1-Q22.2 DELETION.

Porfirio M, Lo-Castro A, et al.

Objective: In this study, we report a single case of a young male with attention-deficit-hyperactivity disorder (ADHD), oppositional defiant disorder (ODD), eating disorder, excessive weight and mild mental retardation seen in association with a de novo deletion of 2q21.1-q22.2.

Design: Case report. A patient with a de novo deletion of 2q21.1-q22.2 was evaluated on a number of occasions over a 5-year period, using physical and neuropsychological examination and laboratory investigations. His behavioural symptoms satisfied criteria for ADHD and ODD, according to DSM-IV TR (Text Revised). Wechsler Intelligence Scale for Children- Revised (WISC-R) documented that he had a total IQ of 61. He presented with repeated binge eating episodes and significant weight gain. Dysmorphological examination revealed subtle abnormal features. EEG, brain MRI, cardiac examination, ECG, pubertal staging and laboratory investigations were normal. He started pharmacological treatment with methylphenidate (MPH; Novartis, Basel, Switzerland), with benefit seen in his behavioural problems, but without appetite control. Karyotype revealed an apparently balanced translocation, involving chromosomes 1 and 2. Array comparative genomic hybrid- ization (aCGH) analysis detected a de novo cryptic deletion of 2q21.1-q22.2 bands (12.6Mb).

Conclusion: To our knowledge, this is the first report of a clinical phenotype associated with this chromosomal abnormality. In a large sample genome-wide linkage study, a susceptibility locus for ADHD was found at the 2q21.1 region. The deletion encompasses several genes with a putative role in different domains of behavioral control and neurocognitive functioning.

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Psychiatry Res Neuroimaging. 2012;202:245-51.

WHITE MATTER ABNORMALITIES ASSOCIATED WITH DISRUPTIVE BEHAVIOR DISORDER IN ADOLESCENTS WITH AND WITHOUT ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.

Wang Y, Horst KK, Kronenberger WG, et al.

Disruptive behavior disorders (DBD) are among the most commonly diagnosed mental disorders in children and adolescents. Some important characteristics of DBD vary based on the presence or absence of comorbid attention-deficit/hyperactivity disorder (ADHD), which may affect the understanding of and treatment decision-making related to the disorders. Thus, identifying neurobiological characteristics of DBD with comorbid ADHD (DBD. +. ADHD) can provide a basis to establish a better understanding of the condition. This study aimed to assess abnormal white matter microstructural alterations in DBD. +. ADHD as compared to DBD alone and healthy controls using diffusion tensor imaging (DTI). Thirty-three DBD (19 with comorbid ADHD) and 46 age-matched healthy adolescents were studied using DTI. Fractional anisotropy (FA), and mean diffusivity (MD), radial diffusivity (RD) and axial diffusivity (AD) were analyzed using tract-based spatial statistics (TBSS). Significantly lower FA and higher MD, RD and AD in many white matter fibers were found in adolescents with DBD. +. ADHD compared to controls. Moreover, lower FA and higher RD were also found in the DBD. +. ADHD versus the DBD alone group. Alterations of white matter integrity found in DBD patients were primarily associated with ADHD, suggesting that ADHD comorbidity in DBD is reflected in greater abnormality of microstructural connections.

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Psychological Services. 2012 Aug;9:293-97.

TELEMEDICINE AND ADHERENCE TO NATIONAL GUIDELINES FOR ADHD EVALUATION: A CASE STUDY.

Nelson EL, Duncan AB, Peacock G, et al.

The pilot project evaluated a telemedicine clinic's adherence to American Academy of Pediatrics (AAP) guidelines for attention-deficit/hyperactivity disorder (ADHD) evaluation. Real-time videoconferencing linked the patients, the families, and the specialty mental health team. The ADHD Telemedicine Clinic adherence to AAP guidelines was tracked using chart data. The study included 22 patients (Mean age = 9.3 years, SD = 2.3 years) participating in 69 telemedicine visits across 13 different school-related sites. The ADHD Telemedicine Clinic reached extremely high adherence rates across the AAP evaluation guidelines for ADHD, ranging from 95–100% across the six guidelines. No factor inherent to the telemedicine service delivery mechanism impeded adherence to national guidelines for ADHD evaluation. Telemedicine-based outreach had the greatest impact on AAP Guideline #4, stating that information should be obtained from the child's academic setting. The school-based telemedicine clinic allowed increased communication across the school and specialty mental health systems and facilitated greater input across child, parent, school personnel, and mental health professionals.

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Psychological Services. 2012 Aug;9:320-22.

TELEHEALTH FOR UNDERSERVED FAMILIES: AN EVIDENCE-BASED PARENTING PROGRAM.

Reese RJ, Slone NC, Soares N, et al.

Families with a child diagnosed with attention-deficit hyperactivity disorder completed an 8-session parenting program, the Group Triple P Positive Parenting Program, provided by videoconferencing technology. Families reported improved child behavior (effect size of d = -1.23) and decreased parent distress (d = -0.34). Parent training implemented with videoconferencing technology can be an effective way of delivering evidence-based services to families with specialized needs.

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Remedial and Special Education. 2012 Jul;33:258-68.

IMPROVING THE READING RECALL OF HIGH SCHOOL STUDENTS WITH ADHD .

Johnson JW, Reid R, Mason LH.

Students with attention-deficit/hyperactivity disorder (ADHD) often have difficulty with reading comprehension. This multiple baseline across participants design with multiple probes study examined the effectiveness of a multicomponent reading comprehension strategy (TWA: Think Before Reading, Think While Reading, Think After Reading) taught following the self-regulated strategy development model on social studies expository text recall of three high school students with ADHD. Results showed improvement in the number of main ideas and percentage of supporting details recalled. Gains were maintained and some improvement occurred at 2- and 4-week follow-ups. Implications for future research and practice are discussed.

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Res Dev Disabil. 2012;33:2292-300.

CAN PSYCHOPATHOLOGY AT AGE 7 BE PREDICTED FROM CLINICAL OBSERVATION AT ONE YEAR? EVIDENCE FROM THE ALSPAC COHORT.

Allely CS, Doolin O, Gillberg C, et al.

One of the challenges of developmental psychopathology is to determine whether identifiable pathways to developmental disorders exist in the first months or years of life. Early identification of such disorders poses a similar challenge for clinical services. Using data from a large contemporary birth cohort, we examined whether psychopathology at age seven can be predicted from clinician observation at one year. Two groups of clinical raters observed videos of caregiver-infant interaction. Neither group of raters could reliably identify any precursors of later development of psychopathology in the one-year-old infants in this setting.

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Somnologie. 2012;16:118-24.

SUBTYPES OF ADHD AND THEIR ASSOCIATION WITH SLEEP DISTURBANCES IN CHILDREN.

Wagner J, Schlarb AA.

Objective. So far, little is known about potential links between subtypes of attention deficit hyperactivity disorder (ADHD) and sleep disturbances in childhood. There fore, this study examined the association between sleep disorders and all three subtypes of ADHD.

Methods. A total of 60 children showing attention deficit symptoms (aged 6-13 years; 88.3% boys) were diagnosed with regard to ADHD according to the DSM-IV-TR. The subtypes of ADHD diagnosed were then related to potential sleep disturbances as measured using a standardized parent-rated questionnaire (Children's Sleep Habits Questionnaire, CSHQ-DE).

Results. Clinically significant elevated scores in the CSHQ-DE's Sleep Disturbance Scale were exhibited in all 60 children. Parents of the children with primarily hyperactive-impulsive subtype reported the highest scores. Children with this subtype displayed the highest rate of specific sleep disorders, e.g., increased daytime sleepiness and higher bedtime resistance.

Conclusion. The assumption that children with ADHD show elevated scores of sleep disturbances was verified. In addition, it was possible to identify a unique pattern of sleep disturbances corresponding to the respective ADHD subtypes.

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Wiad Psychiatr. 2012;15:37-44.

SUGGESTIONS OF INTERVENTIONS BASED ON SYSTEMIC THINKING IN CHILDREN AND ADOLESCENTS WITH ADHD DIAGNOSIS.

Cwojdzinska A.

This paper aims to present the possible consequences of the application of systemic thinking in working with children and adolescents with ADHD diagnosis and their families. Systemic thinking is the basic theoretical frame for systemic therapy and is based on the theory of social constructivism and systems theory. The relationship of systemic therapy theory to the diagnosis, as a theoretical construct, and its potential consequences is discussed. Systemic therapist's working philosophy was presented in the context of the problem of hyperactivity, which aims at creative interaction with the client and family in order to increase the number of possible solutions. The main part of the article is an overview of examples of interventions that may be used in working with children and adolescents with ADHD diagnosis and/or their families.

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Yeni Symp. 2012;50:76-82.

EFFECT OF PARENTAL TEMPERAMENT AND CHARACTER TRAITS IN CHILDREN WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER AND OPPOSITIONAL DEFIANT BEHAVIORS.

Genco Usta M, Turkbay T, Congologlu A.

Objective: Attention deficit hyperactivity disorder (ADHD) is one of the most frequent psychiatric disorders of childhood. Oppositional defiant disorder (ODD) frequently shows comorbidity with ADHD. The aim of this study to investigate the relationship between ADHD related symptoms (attention deficiency, hyperactivity, oppositional behaviors etc.) and parental temperament and character traits.

Method: This study consisted of two groups of children that with ADHD only (n=27) and ODD with ADHD (n=22), and their parents. Correlations between ADHD symptoms and behavioral problems of children with parent temperament and character traits investigated by parent reported scales.

Findings: We found that ADHD/ODD group had externalizing behavioral problems higher than ADHD only group, and these relations between child ADHD symptoms and parents' temperament-character traits were showed. Mothers of ODD with ADHD group had higher harm avoidance scores than ADHD only group. There were significant correlations between mothers' self-transcendence scores and children's internalizing behavioral problems.

Discussions and Conclusions: We suggest that parents' temperament and character traits may have effects development of ADHD and ODD comorbidity, particularly with mothers' harm avoidance scores. Also parent temperamental traits have possible effects on reporting styles in children's behavior rating scales, thus it is important for clinical practices.

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Z Kinder- Jugendpsychiatr Psychother. 2012;40:287-300.

THE MEDICAL TREATMENT OF ATTENTION DEFICIT HYPERACTIVITY DISORDER (ADHD) WITH AMPHETAMINES IN CHILDREN AND ADOLESCENTS.

Frolich J, Banaschewski T, Spanagel R, et al.

Introduction: Psychostimulants (methylphenidate and amphetamines) are the drugs of first choice in the pharmacological treatment of children and adolescents with attention deficit hyperactivity disorder (ADHD).

Objective: We summarize the pharmacological characteristics of amphetamines and compare them with methylphenidate, special emphasisis being given to a comparison of effects and side effects of the two substances. Finally, we analyze the abuse and addiction risks.

Methods: Publications were chosen based on a Medline analysis for controlled studies and meta-analyses published between 1980 and 2011; keywords were amphetamine, amphetamine salts, lisdexamphetamine, controlled studies, and metaanalyses.

Results and Discussion: Amphetamines generally exhibit some pharmacologic similarities with methylphenidate. However, besides inhibiting dopamine reuptake amphetamines also cause the release of monoamines. Moreover, plasma half-life is significantly prolonged. The clinical efficacy and tolerability of

amphetamines is comparable to methylphenidate. Amphetamines can therefore be used if the individual response to methylphenidate or tolerability is insufficient before switching to a nonstimulant substance, thus improving the total response rate to psychostimulant treatment. Because of the high abuse potential of amphetamines, especially in adults, the prodrug lisdexamphetamine (Vyvanse) could become an effective treatment alternative. Available study data suggest a combination of high clinical effect size with a beneficial pharmacokinetic profile and a reduced abuse risk.
Conclusions: In addition to methylphenidate, amphetamines serve as important complements in the psychostimulant treatment of ADHD. Future studies should focus on a differential comparison of the two substances with regard to their effects on different core symptom constellations and the presence of various comorbidities.

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Aripiprazole in Children with Tourette's Disorder and Co-morbid Attention-Deficit/Hyperactivity Disorder: A 12-Week, Open-Label, Preliminary Study

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Abstract

Tourette's disorder (TD) in children and adolescents is frequently co-morbid with attention-deficit/hyperactivity disorder (ADHD). Dopamine-blockers are the first line treatment for TD, whereas dopamine-agonists, such as stimulants, are the gold-standard in the treatment of ADHD. These contrasting effects supported concerns about the risk that stimulants for treating ADHD may trigger or worsen co-morbid tics. Aripiprazole, a partial dopamine agonist, acts as an antagonist at dopamine D2 receptors in hyperdopaminergic conditions and displays agonist properties under hypodopaminergic conditions. The present study describes the use of aripiprazole (10.0±4.8 mg/day) in a consecutive group of 28 patients with a primary diagnosis of TD and co-morbid ADHD, combined subtype. The Yale Global Tic Severity Scale (YGTSS) and the ADHD-Rating Scale (ADHD-RS-IV) were used as primary outcome measures and both significantly improved ($p < 0.001$) after the treatment. Global measures of severity (Clinical Global Impressions–Severity) and of functional impairment (Children's Global Assessment Scale) also significantly improved during the treatment ($p < 0.001$). At the YGTSS there was a reduction of 42.5%, in motor tics, of 47.9% in phonic tics (44.7% for the combined scores), and of 32.3% in tic impairment. Nineteen patients (67.9%) had a reduction of at least 50% of the YGTSS score (motor+phonic tics). The improvement at the ADHD-RS-IV score was 22.5%, 12 patients (42.8%) presented an improvement of 30%, but only 2 (7.1%) an improvement greater than 50%. Using a logistic regression model, a reduction of at least 30% in ADHD-RS-IV score was more likely to occur in the obsessive-compulsive disorder co-morbid group. Aripiprazole was well tolerated and none of the patients discontinued medication because of side effects. In summary, aripiprazole resulted in an effective treatment for TD, but it was only moderately effective on co-occurring ADHD symptomatology. Our preliminary data suggest that aripiprazole may represent a possible therapeutic option, among other possible monotherapies addressing both tics and ADHD.

Introduction

TOURETTE'S DISORDER (TD) is a neurodevelopmental disorder with multiple vocal and motor tics (American Psychiatric Association 2000). TD is frequently co-morbid with other disorders involving the basal ganglia, including attention-deficit/hyperactivity disorder (ADHD) and obsessive-compulsive disorder (OCD) (Palumbo et al. 1997; Grados and Mathews 2008). In a large sample of 596 subjects with TD, only 24% presented TD only, whereas 32% had TD plus OCD, 10% TD plus ADHD, and 34% TD plus both ADHD and OCD (Grados and Mathews 2008). Data from Medicaid (n=10.247.827) and privately insured youths (n=16.128.828) focusing on tic disorder diagnoses in 4–18 year-olds during a 1-year period, reported a rate of ADHD co-morbidity of 50.2% and 25.9%, respectively (Olfson et al. 2011).

Dopaminergic modulation is a crucial component in both motor and vocal tics and ADHD symptoms, but with contrasting mechanisms. Traditionally, dopamine-blockers are the first line treatment for tics and have the most compelling evidence of efficacy from controlled studies (Du et al. 2010). On the contrary, dopamine-agonists, such as stimulants, are the gold-standard in the treatment of ADHD (Kaplan and Newcorn 2011). These contrasting effects supported concerns about the risk that stimulants for treating ADHD may trigger or worsen co-morbid tics (Cohen et al. 1982; Robertson and Eapen 1992). However, several studies have shown

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that stimulants are quite effective in controlling ADHD even in the context of TD and they do not inevitably worsen motor or vocal tics (Tourette's Disorder Study Group 2002). A recent meta-analysis (including nine studies and 477 subjects) analyzed the relative efficacy of different medications in children with both TD and ADHD (Bloch et al. 2009). Methylphenidate resulted in the best and most rapid treatment for ADHD and it did not worsen tic severity, at least in the short term. Atomoxetine has been explored as a non-stimulant treatment for ADHD patients with co-morbid TD, with positive effects on ADHD but only mild improvements in tic symptomtology (Spencer et al. 2008). Further, some case studies reported possible recurrences of tics during or following treatment with atomoxetine (Párraga et al. 2007; Sears and Patel 2008).

Alpha-2 agonists (clonidine and guanfacine), which decrease the firing of noradrenaline neurons in locus ceruleus (Scahill 2009), can offer a combined improvement in both tic and ADHD symptoms (Bloch et al. 2009). Clonidine can be effective in both children with TD (Du et al. 2008; Hedderick et al. 2009) and ADHD (Jain et al. 2011), with possible improvements in hyperactivity, impulsiveness, and inattention in children with tic disorders. Also guanfacine significantly improves ADHD symptoms in children with tic disorders (Scahill et al. 2001). However, both clonidine and guanfacine are associated with sedation, fatigue, somnolence, and modest reductions in heart rate and blood pressure (Scahill 2009). A consensus ADHD algorithm for ADHD in TD patients, suggests starting with psychostimulants, followed by atomoxetine or clonidine/guanfacine (Pliszka et al. 2006). In addition, the possibility of a co-therapy with a stimulant and an antipsychotic should also be mentioned, even though this association may be poorly tolerated (Benjamin and Salek 2005; Hollis and Thompson 2007).

Aripiprazole is a newer antipsychotic with a specific mechanism, being a partial dopamine agonist, acting as an antagonist at dopamine D2 receptors in hyperdopaminergic conditions, and displaying agonist properties under hypodopaminergic conditions. Further, it acts as a partial agonist of 5-HT_{1A} receptor and antagonist of $5HT_{2A}$ receptor (Burris et al. 2002). Based on animal models, it has been proposed that the agonist effect on 5-HT_{1A} receptor may explain the anti-OCD properties of aripiprazole (Matsushita et al. 2005), compared to other atypical antipsychotics, whose potent $5HT_{2A}$ antagonism may even worsen OCD symptoms (Gao et al. 2006).

Efficacy and fair tolerability of aripiprazole in youths with TD is supported by several noncontrolled studies or case reports since 2005 (Yoo et al. 2007; Budman et al. 2008; Seo et al. 2008; Lyon et al. 2009; Murphy et al. 2009; Cui et al. 2010; Yoo et al. 2011). Budman et al. (2008) treated 37 patients, 8 of which (22%) discontinued treatment because of side effects (weight gain, akathisia, sedation). The remaining 29 youths, who completed the 12-week trial with a mean aripiprazole dosage of 12.3 ± 7.5 mg/day, improved tic symptomatology (and in all but one their explosive outbursts). In Cui et al. study (2010), 72 children and adolescents participated in an 8-week, open-label trial and showed, at the end point, a 50.3% reduction at the Yale Global Tic Severity Scale (YGTSS), with improvement of behavior symptoms according to Child Behavior Checklist (Achenbach and Edelbrock 1983), and without weight gain. Finally, in a nonrandomized, parallel-group study comparing aripiprazole (n = 31) (up to a maximum 20 mg/day) and haloperidol (n = 17) (up to a maximum 4.5 mg/day), the two medications showed similar efficacy (rate of response 54.3% with aripiprazole, 63.4% with haloperidol) (Yoo et al. 2011). In this study, only 16% in the aripiprazole group, compared to 35.3% in the haloperidol group, discontinued treatment because of unbearable side effects. Aripiprazole as effective augmenting strategy has been explored in youths with OCD who did not respond to serotonin-selective reuptake inhibitor (SSRI), with an additional positive effect on co-morbid tic disorder (Masi et al. 2010).

Evidence supporting efficacy of aripiprazole on ADHD symptoms is more controversial. Findling and colleagues (2008) explored efficacy of aripiprazole (maximum dose 10 mg/day) in a 6-week, open-label pilot trial including 23 youths, aged 8–12 years with a primary diagnosis of ADHD (14 combined and 9 predominately inattentive subtype). A significant improvement from the baseline was found on clinical measures, ADHD-Rating Scale (ADHD-RS) (DuPaul et al. 1998), Clinical Global Impressions (CGI) (Guy 1976), and Children Global Assessment Scale (C-GAS) (Shaffer et al. 1983). Aripiprazole treatment improved both inattentive and hyperactive symptoms and overall functioning for patients with either the inattentive or the combined subtype of ADHD. Sedation was frequently reported (n = 18; 78.3%), but aripiprazole did not have a negative impact on cognitive functioning (Conners' Continuous Performance Test, Reading and Math Fluency, Stroop Color and Word Test).

The present study describes the use of aripiprazole in a consecutive group of patients with a primary diagnosis of TD and co-morbid ADHD, combined subtype, who received aripiprazole for 12 weeks. Efficacy was separately assessed for tic and ADHD symptoms.

Methods

Sample

This is a study based on a clinical database of 28 consecutive patients diagnosed as having TD and co-morbid ADHD (combined subtype), referred to two different tertiary-care hospitals by other hospitals, community-based child psychiatrists or pediatricians, to assess the need for pharmacotherapy. The 28 patients were aged between 8 and 16 years (mean age 12.1 ± 2.3 years, mean age at onset of TD 7.8 ± 1.6 years, 26 males and 2 females). The inclusion criterion for this study was the fulfillment of the **Diagnostic and Statistical Manual of Mental Disorders**, 4th edition (DSM-IV) (American Psychiatric Association 1994) criteria for TD and ADHD, including duration, and impairment (CGI–Severity [CGI-S] score 4 or less; C-GAS score 60 or less), based on a structured clinical interview according to DSM-IV criteria, the Schedule for Affective Disorders and Schizophrenia for School-Age Children–Present and Lifetime Version (K-SADS-PL) (Kaufman et al. 1997). Further, all the patients scored 30 or higher at the YGTSS (Leckman et al. 1989), and 30 or higher at the ADHD-RS-IV.

All patients with mental retardation, pervasive developmental disorders, schizophrenia, or neurological diseases (epilepsy, brain injuries, or cerebral lesions documented by magnetic resonance imaging) were excluded.

Demographic, clinical, and therapeutic features are reported in Table 1.

Measures

The K-SADS-PL (Kaufman et al. 1997) was individually administered to the parents and to the patients, by child psychiatrists trained in the use of this interview. The K-SADS-PL is a structured interview according to DSM-IV, organized in such a way as to explore the presence or absence of each of the symptoms in different psychiatric syndromes.

TABLE 1. BASELINE DEMOGRAPHIC, CLINICAL, AND TREATMENT CHARACTERISTICS OF CHILDREN AND ADOLESCENTS WITH GILLES DE LA TOURETTE'S DISORDER AND CO-MORBID ATTENTION-DEFICIT/HYPERACTIVITY DISORDER ($N = 28$)

Males, *n* (%)	26 (92.9)
Age, mean (SD)	12.1 (2.4)
Age at onset of Tourette's disor., mean (SD)	7.8 (1.6)
Aripiprazole dosage, mg/day	10.0 (4.8)
Responders, Tourette's disorder, *n* (%)	19 (67.9)[a]
Responders, ADHD, (< 30%) *n* (%)	12 (42.8)[b]
Responders, ADHD, (< 50%) *n* (%)	2 (7.1)[c]
Co-morbidity, *n* (%)	
Generalized anxiety disorder	4 (14.3)
Panic disorder	1 (3.6)
Social phobia	4 (14.3)
Simple phobia	1 (3.6)
Obsessive-compulsive disorder	12 (42.9)
Oppositional defiant disorder	5 (17.9)
Conduct disorder	2 (7.1)
Pharmacotherapy, *n* (%)	
SSRI	5 (17.9)
Psychotherapy, *n* (%)	17 (60.7)

[a]50% Reduction of YGTSS from the baseline.
[b]Reduction of 30% of ADHD-RS-IV.
[c]Reduction of 50% of ADHD-RS-IV.
SD = standard deviation; ADHD = attention-deficit/hyperactivity disorder; SSRI = serotonin-selective reuptake inhibitor; YGTSS = Yale Global Tic Severity Scale; ADHD-RS = ADHD-Rating Scale.

The severity of global impairment at baseline and subsequent course during follow-up were assessed monthly by means of the CGI-S and CGI–Improvement scores (CGI-I) (Guy 1976). CGI-S Score is a single item, recorded at the baseline, that rates the severity of global symptomatology on a scale from 1 (''Normal'') to 7 (''Extremely ill''). CGI-I Score is a single item, recorded during the follow-up, that rates behavior from 1 (''Very Much Improved'') to 7 (''Very Much Worsened''). Further, global functional impairment was assessed with the C-GAS (Shaffer et al. 1983) that describes the severity of functional impairment on a scale from 0 (severe impairment) to 100 (superior functioning).

ADHD was explored using the ADHD-RS-IV, a widely used measure of efficacy in clinical trials of ADHD treatments in children and adolescents, derived from the 18 inattentive and hyperactive/impulsive diagnostic criteria for ADHD from DSM-IV (DuPaul et al. 1998).

Current tic symptomatology (vocal and phonic) was assessed with the YGTSS (Leckman et al. 1989), a semi-structured clinical interview with three summary tic scores (total motor, total phonic, total tic) and an impairment scale.

Extrapyramidal side effects were explored by using the Abnormal Involuntary Movement Scale (AIMS) (NIMH 1985).

Primary outcome measures were YGTSS and ADHD-RS-IV at the baseline and at the end point (12 weeks). Further, we considered as a response criterion for TD, a 50% reduction of YGTSS from the baseline. Given that the effect of antipsychotics on tics is well established, although the effect of aripiprazole on ADHD is only putative, both a reduction of 30% and 50% of ADHD-RS-IV were considered as response criteria, to explore both a good and a moderate effect of medication on ADHD symptomatology.

Treatments

All the 39 adolescents received aripiprazole. The titration of aripiprazole was the following. The starting dose of aripiprazole was 1.25 or 2.5 mg in the morning, with subsequent titration of 2.5 mg no more than at 5-day intervals, depending on clinical outcome and occurrence of side effects, but frequently with longer intervals, according to the clinicians' judgments, to better assess the TD response. The maximum dosage was the highest dose associated with a good tolerability and efficacy, with an upper limit of 20 mg/day.

The patients received the medication in the morning and at bedtime. When sleeping disorders were reported, medication was given in the morning and/or at lunchtime.

Five patients were drug-naïve, the other 23 had received previous treatment with antipsychotics (risperidone, pimozide, haloperidol) without significant efficacy or side effects (extrapiramidal side effects and/or weight gain and/or sedation). Five patients previously received methylphenidate, but the medication was discontinued because of worsening of tics. Two of these children also previously received atomoxetine, without improvement of ADHD symptoms and no efficacy on TD. At baseline, all patients were drug-free for at least 1 week.

Five of the 12 patients with co-morbid OCD received an SSRI during the study. Given that SSRIs are not considered an effective treatment for both TD and ADHD, we assumed that this co-therapy did not affect tic and ADHD response to aripiprazole. Seventeen patients (60.7%) were receiving a co-occurring cognitive behavioral therapy at the baseline.

Subjects and parents received detailed information on the characteristics of the assessment instruments and different treatment options; all parents gave a written informed consent, and all the patients gave their consent as well.

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 an unpaired t-test on continuous variables. Considering the large number of comparisons, p values were based on two-tailed tests with alpha = 0.001, using a post-hoc Bonferroni correction. The odds ratio and 95% confidence interval (CI) were correlated using logistic regression model. The predictive significance for ADHD and TD response to treatment of the following variables was assessed: age (< 11 vs. ≥ 11), age at onset of TD (< 7 vs. ≥ 7), OCD co-morbidity, co-occurring psychotherapy (combined treatment).

Results

This was a sample of severely impaired patients, in terms of clinical severity (CGI-S = 5.6 ± 1.0) and functional impairment (C-GAS = 42.6 ± 8.2). The most relevant co-morbidity was with OCD (12, that is 42.9%). (Table 1)

The mean aripiprazole dosage was 10.0 ± 4.8 mg/day (range 5–20 mg).

A comparison of baseline and end point scores shows that all the YGTSS scores (number, frequency, intensity, complexity, and interference of both motor and phonic tic) were statistically significant ($p < 0.001$), except for the intensity of phonic tics, whose improvement did not survive Bonferroni correction. Also ADHD-RS-IV total score significantly improved during the treatment ($p < 0.0001$). When the improvement in tic symptomatology was separately assessed for motor and phonic tics and for the impairment, the reduction of the scores was 42.5% for motor tics, 47.9% for phonic tics (44.7% for the combined scores), and 32.3% for tic impairment. The improvement of the ADHD-RS-IV score was 22.5%.

The global measures of severity (CGI-S) and of functional impairment (C-GAS) also significantly improved during the treatment. More specifically, CGI-S improved from 5.6 ± 1.0 at the baseline (severely ill), to 2.7 ± .9 (mild to moderately ill) at the end of the follow-up ($p < 0.0001$).

The rate of responders in TD according to a reduction of at least 50% of the YGTSS score (motor + phonic tics) was 67.9% (19 patients). According to a categorical measure of clinical response, 12 patients (42.8%) presented an improvement of 30% or more at the ADHD-RS-IV, but only 2 (7.1%) an improvement greater than 50%.

Using a logistic regression model, we assessed and found that a reduction of at least 30% of ADHD-RS-IV score was more likely to occur in the OCD co-morbid group (odds ratio 8.333; 95% CI 1.344–51.671, $p < 0.001$). No significant associations occurred for age (< 11 vs. ≥ 11), age at onset of TD (< 7 vs. ≥ 7), and psychotherapy (combined treatment). These possible predictors were not associated with a reduction of YGTSS score of at least 50%.

Aripiprazole was well tolerated with no patients discontinuing medication because of side effects. Six patients (21.4%) experienced mild sedation, four patients (14.3%) mild to moderate agitation, prevalently in the first 2 weeks, four (14.3%) complained of mild and transient nausea, two (2.6%) of increased appetite. One patient had to reduce the aripiprazole dose at week 12 due to mild hand tremor that remitted after decrease of aripiprazole dosage from 7.5 to 5 mg/day. No other patients presented extrapyramidal symptom (EPS) according to the AIMS. No significant effects were revealed in blood parameters, prolactin levels, electrocardiogram, weight, height, blood pressure, and cardiac frequency during the follow-up period. Of note, cognitive functioning did not appear to be negatively impacted by aripiprazole treatment, based on scholastic performance reported on school records.

Discussion

ADHD symptoms are frequently under-recognized in youths with TD, especially when tics are more severe, and often undertreated with stimulants because of concerns about a possible worsening of tics. Although stimulants have not been shown to worsen tics in most people with tic disorders, they may nonetheless exacerbate tics in individual cases (Pringsheim and Steeves 2011). Antipsychotics can be effective in ameliorating tic symptomatology, but the blockade of dopaminergic transmission may further worsen the inattention symptomatology of ADHD. Alpha-adrenergic agents may be effective in improving both tic and ADHD symptoms, but they are sometimes only moderately effective in TD, compared to antipsychotics. There is still limited evidence suggesting that aripiprazole, based on its partial dopamine agonism, may be effective in the treatment of tics and it may also ameliorate ADHD symptoms.

Our data indicate that aripiprazole is effective in reducing tic symptoms, with an improvement of both motor and vocal tics, except for intensity of phonic tics. However, number, complexity, and interference of phonic tics significantly improved. The reduction of combined motor and phonic tics was 44.7%. The impairment deriving from TD was also significantly improved by aripiprazole. About two-thirds of the youths experienced a significant improvement in tic symptomatology (improvement of at least 50% of total YGTSS score).

Regarding ADHD symptomatology, aripiprazole is only moderately effective. Although the ADHD-RS-IV score significantly improved after treatment, the improvement was only 22.5%. Further, 42% of the patients presented an improvement greater than 30% at the ADHD-RS-IV, but only 7.1% of the patients showed an improvement greater than 50%. When selected predictors of clinical response were considered for TD and ADHD, only OCD co-morbidity was associated with a better response to ADHD symptoms (improvement of at least 30% of ADHD-RS-IV score). This finding may be related to the possible improvement of OCD symptoms after aripiprazole treatment (Masi et al. 2010) with secondary beneficial effects on attention. Not alternatively, the ADHD-OCD association may represent a specific pattern of co-morbidity, with greater incidence in males, an earlier onset of OCD, a greater psychosocial impairment, and a heavier co-morbidity (tic disorders, bipolar disorder, oppositional defiant disorder/conduct disorder) (Geller et al. 2002; Masi et al. 2006). The co-morbidity among ADHD, OCD, and Tourette's disorder, based on the partial overlap of neurobiological basis of these disorders (Grados and Mathews 2008) is more often characterized by a higher frequency of aggressive behavior and explosive outbursts of rage, independent of tic severity or age (Stephens and Sandor 1999), with putative sensitivity to specific treatments, such as aripiprazole.

The lower improvement in ADHD symptomatology may be partly affected by the dosage of aripiprazole, which was relatively high (10 ± 4.8 mg/day), in order to adequately improve tic symptoms. Lower dosages may be more beneficial for ADHD symptoms, as they are associated with higher dopamine agonism. Optimal dosages for TD and ADHD may be thus different, and an accurate balance between higher and lower aripiprazole dosages may be one of the main focuses of treatment of these patients.

When the effectiveness of treatment was assessed with global measures of clinical severity and functional impairment (such as CGI-S and C-GAS), patients presented a positive response in their overall symptomatology and impairment. This is relevant, considering that aripiprazole was well tolerated in terms of both side effects and cognitive functioning. However, the short duration of the follow-up limits strong conclusions on safety, namely on weight gain or EPS, which may appear later in the course of treatment.

This study should be considered in light of several methodological limitations. First of all, our results are not based on a randomized, placebo-controlled study, but on an open study on a small sample, and this limits evaluation of response. Thus our findings should be considered preliminary. Further, there is no comparison to other active treatments of TD + ADHD, such as stimulants alone, or stimulants plus antipsychotics. Finally, the short duration of the follow-up limits conclusions of long-term efficacy and safety, particularly on EPS and weight gain. However, our findings describe an unselected sample of children and adolescents with TD and co-morbid ADHD. Clinical open studies, albeit not controlled, might represent a helpful source of information regarding the effectiveness of a treatment under more ordinary clinical conditions.

Conclusions

Our findings indicate that aripiprazole monotherapy is effective on tic symptoms, with similar improvements in both motor and phonic tics, and on functional impairment. The effective dosage of aripiprazole is relatively high (10.0 ± 4.8 mg/day). On the contrary, the response of the symptoms of ADHD is only moderate, and it does not approach that seen with stimulants or even atomoxetine. A positive predictor of response to ADHD symptoms is the co-morbidity with OCD. At least in the first 12 weeks of treatment, aripiprazole is well tolerated, in particular on weight gain and EPS. Further research is needed to support these data with randomized,

placebo-controlled studies with larger samples. Further, studies addressing the optimal dosages of aripiprazole for both tics and ADHD symptoms may indicate a more effective titration strategy.

Clinical Significance

Co-morbid ADHD in patients with TD is far from rare, and it can strongly affect the clinical picture, resulting in a more severe impairment of quality of life, psychosocial outcome, and social competence (Hoekstra et al. 2004; Roessner et al. 2007). Similarly, tics are a strong indicator of a more severe psychopathology in ADHD patients and their management should be considered a priority (Schneider et al. 2009). For this reason, both the disorders must be considered in the treatment plan, including the choice of the pharmacotherapy. A possible strategy is a combined treatment aimed at controlling TD and ADHD with distinct medications (i.e., antipsychotics for TD, stimulants for ADHD), with higher rates of efficacy, but with higher risks of side effects, particularly dyskinesias and dystonias (Benjamin and Salek 2005; Hollis and Thompson 2007). An alternative strategy is to consider a monotherapy with medications having at least a putative efficacy on both TD and ADHD (Singer 2010). Aripiprazole monotherapy may be considered as a possible option when tic disorder is the prevalent component of the clinical picture, and/or when a previous treatment with stimulants determined a worsening of tic symptomatology, and/or when alpha(2)-agonists were not effective or poorly tolerated, and/or when an OCD is co-morbid. In these situations aripiprazole may avoid the association between antipsychotics and stimulants. Finally, in patients with a good response on TD but poorer response on ADHD, aripiprazole-stimulants association may be more effective on ADHD symptoms and better tolerated than the association between stimulants and other first- or second-generation antipsychotics, with potential negative impact on cognition.

Disclosures

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202 Brief report

Attention-deficit hyperactivity disorder and binge eating disorder in a patient with 2q21.1–q22.2 deletion

Maria Cristina Porfirio[a], Adriana Lo-Castro[a], Grazia Giana[a], Silvia Giovinazzo[a], Diane Purper Ouakil[b], Cinzia Galasso[a] and Paolo Curatolo[a]

We report the case of a young male with attention-deficit hyperactivity disorder, oppositional defiant disorder, eating problems and overweight, and mild mental retardation. Karyotype analysis detected an apparently balanced translocation: t(1;2)(p34.1;q21.1) *de novo*. Array comparative genomic hybridization analysis defined a de-novo cryptic deletion of 2q21.1–q22.2 bands. The deletion, here first associated with this complex phenotype, encompasses several genes with a putative role in different domains of behavioral control and neurocognitive functions; their deregulated expression may influence metabolic pathways and the role of dopamine in reward, explaining the complex psychiatric phenotype and the pharmacotherapy response described in our patient. *Psychiatr Genet* 22:202–205 © 2012 Wolters Kluwer Health | Lippincott Williams & Wilkins.

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Keywords: attention-deficit hyperactivity disorder, binge eating disorder, chromosome 2, interstitial deletion, methylphenidate, obesity

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Introduction

Attention-deficit hyperactivity disorder (ADHD) is a heterogeneous neurobiologic disorder, characterized by a high level of inattention and hyperactivity/impulsivity, that affects about 5% of school-aged children, with severe outcomes throughout life (Biederman *et al.*, 2008; Curatolo *et al.*, 2009).

Although the disorder is highly heritable, common genetic variants that have been identified to date in genetic association studies only account for a small proportion of variance phenotype. Genetic and environmental hypotheses that implicate the dopamine system and reward/motivation deficits have been described in ADHD.

ADHD may be a risk factor for the development of substance abuse and other psychiatric problems (Biederman *et al.*, 2008). Recently, several clinical and epidemiological evidences have substantiated a possible link between ADHD, overweight/obesity, and eating behavior problems, such as binge eating disorder (BED), both in children and in adults (Cortese *et al.*, 2008; Volkow *et al.*, 2009).

Here, we describe a young male with ADHD, oppositional defiant disorder, binge eating symptoms, and mild mental retardation, in whom the karyotype analysis showed an apparently balanced translocation t(1;2)(p34.1;q21.1) *de novo*. Array comparative genomic hybridization (aCGH) led to the identification of a de-novo cryptic deletion of 2q21.1–q22.2 bands.

Case report

The patient is a 16-year-old boy, first-born of healthy nonconsanguineous parents. The younger child is healthy and the family history was reported to be negative by the parents for psychiatric diseases and eating disorders. The patient was born at 36 weeks of gestation by a spontaneous vaginal delivery after an uneventful pregnancy. Birth weight was 2890 g (50th centile) and Apgar scores were 8 and 9 at 1 and 5 min, respectively. Neonatal physical examination revealed hypotonia. He was mildly delayed in motor and language milestones.

At our first evaluation, he was 12 years old and showed severe hyperactivity, impulsivity, aggressive and disruptive symptoms, sustained attention deficit, oppositional behaviors, clumsiness, and poor social skills. These symptoms appeared from the age of 4 and fulfilled the criteria for ADHD, combined subtype, and oppositional defiant disorder, according to the *Diagnostic and Statistical Manual of Mental Disorders, 4th Text Revision* and Swanson, Nolan and Pelham IV scores. Wechsler Intelligence Scale for Children-Revised showed a total IQ of 61 (verbal IQ = 51, performance IQ = 79). The Leiter International Performance Scale-Revised Attention-Memory Battery pointed out an impairment in attention and memory processes (screener memory = 62; association memory = 86; span memory = 46; attention = 65; memory process = 42).

As the behavioral problems caused significant impairments in family, school, and social settings, the patient started pharmacological treatment with methylphenidate (MPH)-immediate release (40 mg/days; >0.6 mg/kg/days), with clinical improvement.

Risperidone at a maximum dose of 1 mg/days was added at the age of 14, due to a persistence of aggressiveness,

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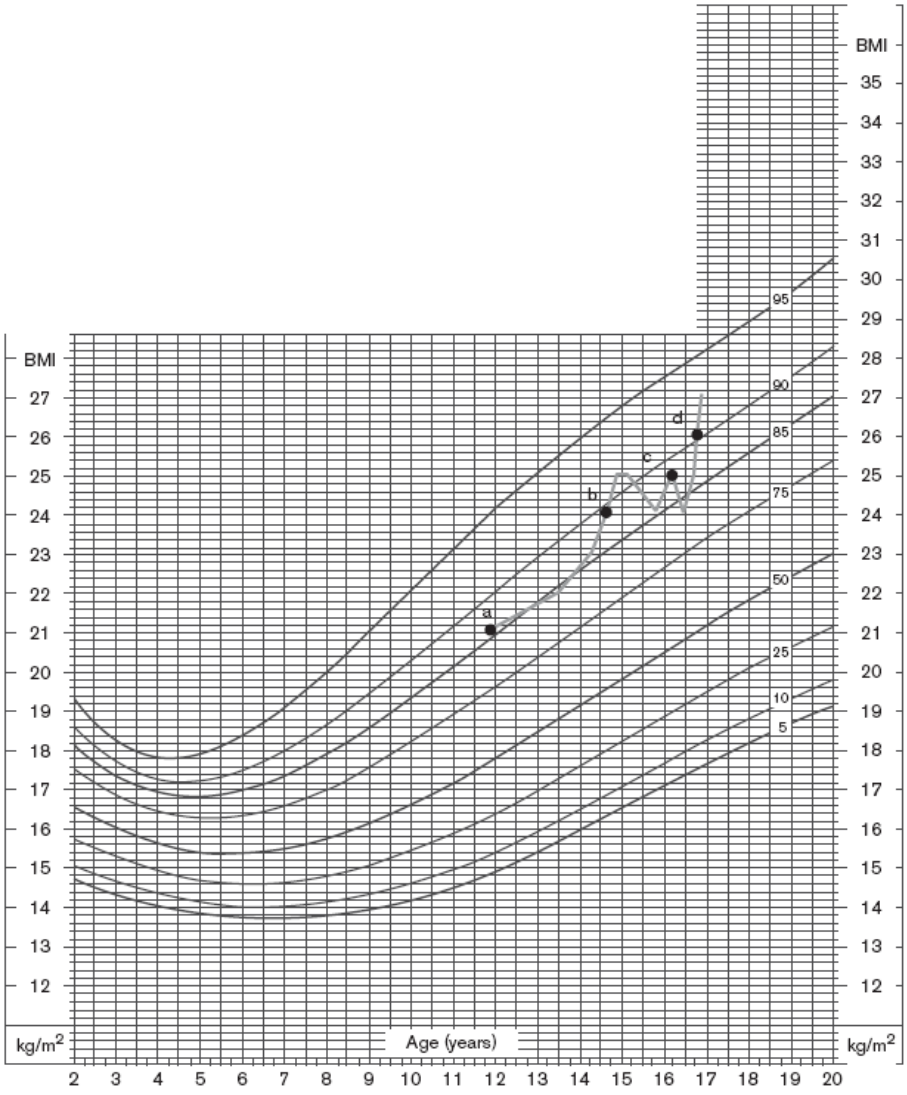
and was discontinued 1 year later because of a lack of a therapeutic effect.

When the patient was 16.5 years old, he showed significant motor instability, impulsivity, and mood dysregulation. Furthermore, he developed abnormal food intake, with binge eating episodes, many times a week, and showed significant weight gain. His weight was 85 kg (90–97th centile), height was 179 cm (75–90th centile), and BMI was 27 (90–95th centile) (Fig. 1). He continued pharmacological treatment with MPH at a dose of 45 mg/day (< 0.6 mg/kg), with a partial beneficial effect on behavioral problems, but without appetite control. Ziprasidone was added, at a dose of 60 mg/days, with an improvement on externalizing symptoms.

Dysmorphological examination revealed a gynoid adipose distribution, a head circumference of 57.7 cm (±2 SD),

Fig. 1



BMI-for-age percentiles, 2–20 years boy. Trend of BMI in our patient (12–17 years of age). (a) Start of treatment with methylphenidate. (b) Start of treatment with risperidone. (c) End of treatment with risperidone. (d) Start of treatment with ziprasidone. Pharmacotherapy did not significantly influence the body weight of the patient. No significant weight loss was reported during methylphenidate treatment (from a to b); no significant weight gain was observed during risperidone treatment (from b to c); a marked increase in weight gain was already observed before the introduction of ziprasidone (from c to d). At the time of our evaluation, the patient was in treatment with methylphenidate and ziprasidone.

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a slightly long face with horizontalized anterior and posterior hairlines, straight and thick eyebrows with synophrys, a broad nose, a long and flat philtrum, a thin upper lip, a narrow palate, low-set ears, large lobes with vertical creases, and bilateral pits on the posterior concha. The parents did not give the permission for publication of the patient's pictures. Our patient showed age-appropriate EEG, brain MRI, cardiac examination, ECG, pubertal development, and findings on laboratory examination (hematological routine, including thyroid functioning and sexual hormones, and urinary parameters) were normal.

Cytogenetic analysis of peripheral blood lymphocytes from the proband was performed using standard techniques, and processed by standard G-banding chromosomes. Karyotype revealed an apparently balanced translocation involving chromosomes 1 and 2: 46,XY t(1;2)(p34.1;q21.1) *de novo* (both parents had normal karyotypes). aCGH analysis was performed on genomic DNA using an oligonucleotide-array with an average resolution of 75 kb (Agilent Technologies, Walldbronn, Germany). DNA was extracted from blood using a commercial Kit (Macherey-Nagel, Duren, Germany). A male DNA was used as the reference (Promega, Madison, Wisconsin, USA). Labeling and hybridization were performed following the manufacturer's protocols (Agilent Technologies, v4.0). Slides were scanned on the Agilent scanner, imaged using Feature Extraction software (v9.5), and analyzed using the CGH analytics software (v4.0.73). The results have been defined using the Database of Genomic Variants (*http://projects.tcag.ca/variation/*). aCGH did not show a gain or a loss of genetic material involving the chromosome 1. A painting fluorescence in-situ hybridization was also performed to exclude the involvement of other chromosomes in the rearrangement, and a specific fluorescence in-situ hybridization BAC clone (RP11–788B24) was used to confirm the deletion on chromosome 2. A 12.6 Mb loss in chromosome bands 2q21.1 and 2q22.2 was found; thus, according to the ISCN 2009 nomenclature, the result was 46,XY.arr (2)(q21.1q22.2)(131,846,327–144,485,540)x1.

Discussion

We describe a patient with severe ADHD plus BED and mild mental retardation. To our knowledge, this is the first report on a similar phenotype associated with a de-novo cryptic deletion of 2q21.1–q22.2 bands.

The interstitial deletions involving 2q21.1 and 2q22.2 bands are quite rare abnormalities, reported in association with various degrees of mental retardation, abnormalities of the central nervous system, other congenital malformations, and Hirschsprung's disease (Shanske *et al.*, 2004). The nine cases reviewed by Shanske *et al.* (2004) do not resemble the dysmorphic traits observed in our patient, except for the presence of ear dimples, which may be a distinctive sign of the syndrome.

In a large sample genome-wide linkage study, a susceptibility locus for ADHD, and in particular for motor timing neuropsychological endophenotype, was found on the 2q21.1 region (Rommelse *et al.*, 2008). Deficits in motor timing processes cause abnormalities in time synchronization and may underlie the impulsiveness and delay aversion observed in ADHD (Rubia *et al.*, 2009).

It has been suggested that the impulsivity and poor inhibitory competences found in patients with ADHD may lead to the development of eating patterns, such as BED, that place youth at an increased risk for overweight/obesity (Cortese *et al.*, 2008). Current findings link both overweight/obesity and ADHD to the dopaminergic pathways and implicate dopamine genes in weight control, eating behaviors, and ADHD, among others (Cortese *et al.*, 2008; Volkow *et al.*, 2009).

The reduction in D2/D3 receptors' availability in accumbens may be related to impaired reward/reinforce pathways, reported in ADHD, and also in abnormal eating habits and obesity. Dysregulation of the hypothalamic–pituitary axis may represent another link between metabolic dysfunctions and psychiatric disorders (Volkow *et al.*, 2009).

In 2q21.1–q22.2, there are several known candidate genes that could explain the phenotype of our patient (Table 1). RAB3 GTPase-activating protein (*RAB3GAP1*) regulates synaptic vesicles' transport in the brain, influencing the neurotransmitter release and synaptic plasticity (Sakane *et al.*, 2006). Single nucleotide polymorphisms of *MGAT5* and *ARHGAP1* genes have yielded evidence for an association with dysinhibitory and addiction behaviors such as alcohol dependence, and conduct disorder, related to altered motivation and dopamine system dysregulation (Dick *et al.*, 2010).

In addition, the *GPR39* gene encodes for a G protein-coupled receptor involved in insulin secretion, gastric emptying, and neurotransmission through the ghrelin/obestatin pathway (Popovics and Stewart, 2011). Although the role of *GPR39* is not yet completely clear, an interesting hypothesis may be that the haploinsufficiency of this gene could lead to a dysregulation of ghrelin-induced activation of mesolimbic dopamine, involved in addictive behaviors such as compulsive overeating (Jerlhag *et al.*, 2010).

Furthermore, *NHPX2* encodes for a signaling protein that binds by α-neurexins. Neurexins and neuroligins play an essential role in synaptic development and transmission, regulating the balance of GABAergic and glutamatergic inputs (Craig and Kang, 2007).

Finally, to the best of our knowledge, we cannot exclude a causal role of long-term epigenetic changes in the development of binge eating disorder. According to an epigenetic hypothesis, both mood dysregulation and eating disorder could be related to the global disturbances in emotion and behavior associated with ADHD. Furthermore, as ADHD is an early-onset behavioral

Table 1 **Potential genetic implications for the phenotype of our patient**

Gene symbol	Gene name	Gene map locus	Possible implications for the psychiatric phenotype
RAB3GAP1 (MIM # 602536)	RAB3 GTPase-activating protein	2q21.3	Regulation of synaptic transmission and plasticity. Inactivating mutations in this gene are associated with Warburg microsyndrome (MIM # 600118) (Sakane *et al.*, 2006)
MGAT5 (MIM # 601774)	α-1,6-Mannosyl-glycoprotein β-1,6-n-acetylglucosaminyltransferase	2q21.3	SNP of the gene has been associated with disinhibitory phenotypes (alcohol dependence, conduct disorder, and suicide attempts) (Dick *et al.*, 2010)
ARHGAP15 (MIM # 610578)	RHO GTPase-activating protein	2q22.2	
GPR39 (MIM # 602886)	G protein-coupled receptor 39	2q21–q22	Implicated in the ghrelin/obestatin pathway, which is associated with dopaminergic reward system and addictive behaviors (compulsive overeating and alcohol dependence) (Jerlhag *et al.*, 2010; Popovics and Stewart, 2011)
NXPH2 (MIM # 604635)	Neurexophilin 2	2q22.1	Signaling molecule that acts by binding to α-neurexins involved in synaptic development and transmission (Craig and Kang, 2007)

The table shows the potential genetic implications for the phenotype of our patient. All these genes are located within 2q21.1 and 2q22.2 bands.
GTP, guanosine 5′-triphosphate; SNP, single nucleotide polymorphism.

disorder, this condition may increase the risk of an obesogenic lifestyle from childhood that might alter the physiological hypothalamic 'set point' related to appetite, weight control, and energy homeostasis. Eating disorder can be seen as developing from learned behaviors, likely arising from epigenetic modifications in the hypothalamic set point, due to a combination of physiological and psychological risk factors (Campbell *et al.*, 2010).

With regard to therapeutic implications, many pharmacological, genetic, and neuroimaging studies suggest that MPH increases the intrasynaptic concentration of dopamine in subcortical brain regions associated with motivation and reward. MPH displays anorexigenic properties, by increasing the dopamine levels in the brain regions involved in food intake circuitries and addiction behaviors.

A limitation of our study is the lack of a molecular characterization of possible disrupted gene(s) on the 1p34.1 region. The loss of function or the positional effect of this gene(s) could play an unknown role in determining the phenotype.

However, the aCGH analysis did not show a gain or a loss of material involving chromosome 1, and our patient showed a good genotype–phenotype correlation.

We hypothesize that the haploinsufficiency of several neighboring genes mapped in 2q21.1–q22 regions and the consequent dysregulation of their functional products may have affected the therapeutic response and the psychiatric comorbidity of our patient.

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Conflicts of interest

There are no conflicts of interest.

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