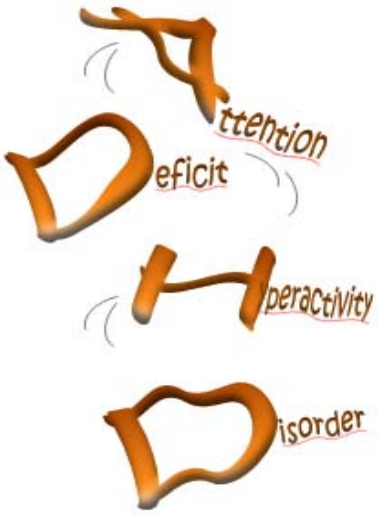
NEWSLETTER



INDICE:

MARIONEGRI
ISTITUTO DI RICERCHE FARMACOLOGICHE

N. 44 anno IV - giugno 2011

BIBIOGRAFIA ADHD GIUGNO 2011

Am Fam Phys. 2011;83:762-68.
ICSI RELEASES GUIDELINE ON DIAGNOSIS AND MANAGEMENT OF ADHD IN CHILDREN.
Armstrong C.

……

Am J Med Genet Part A. 2011;155:1272-80.
11P14.1 MICRODELETIONS ASSOCIATED WITH ADHD, AUTISM, DEVELOPMENTAL DELAY, AND OBESITY.
Shinawi M, Sahoo T, Maranda B, et al.
Genomic copy number imbalances are being increasingly identified as an important cause of intellectual disability and behavioral abnormalities. The typical deletion in WAGR syndrome encompasses the PAX6 and WT1 genes, but larger deletions have been associated with neurobehavioral abnormalities and obesity. We identified four patients with overlapping interstitial deletions on 11p14.1 and extending telomeric to the WAGR critical domain. The minimal overlapping critical chromosomal region was 2.3Mb at 11p14.1. The deletions encompass the BDNF and LIN7C genes that are implicated in the regulation of development and differentiation of neurons and synaptic transmission. All patients with this deletion exhibit variable degrees of developmental delay, behavioral problems, and obesity. Our data show that ADHD, autism, developmental delay, and obesity are highly associated with deletion involving 11p14.1 and provide additional support for a significant role of BDNF in obesity and neurobehavioral problems.

……

……

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.

Arq Neuro-Psiquiatr. 2011 Mar;69:242-52.

ADVANCED TECHNIQUES IN MAGNETIC RESONANCE IMAGING OF THE BRAIN IN CHILDREN WITH ADHD.

Pastura G, Mattos P, Gasparetto EL, et al.

Attention deficit hyperactivity disorder (ADHD) affects about 5% of school-aged child. Previous published works using different techniques of magnetic resonance imaging (MRI) have demonstrated that there may be some differences between the brain of people with and without this condition. This review aims at providing neurologists, pediatricians and psychiatrists an update on the differences between the brain of children with and without ADHD using advanced techniques of magnetic resonance imaging such as diffusion tensor imaging, brain volumetry and cortical thickness, spectroscopy and functional MRI. Data was obtained by a comprehensive, non-systematic review of medical literature. The regions with a greater number of abnormalities are splenium of the corpus callosum, cingulated girus, caudate nucleus, cerebellum, striatum, frontal and temporal cortices. The brain regions where abnormalities are observed in studies of diffusion tensor, volumetry, spectroscopy and cortical thickness are the same involved in neurobiological theories of ADHD coming from studies with functional magnetic resonance imaging.

……..

Behav Ther. 2011;42:449-61.

THE ALLIANCE IN A FRIENDSHIP COACHING INTERVENTION FOR PARENTS OF CHILDREN WITH ADHD.

Lerner MD, Mikami AY, McLeod BD.

The alliance between parent and therapist was observed in a group-based parent-training intervention to improve social competency among children with attention-deficit/hyperactivity disorder (ADHD). The intervention, called Parental Friendship Coaching (PFC), was delivered to 32 parents in small groups as part of a randomized clinical trial. PFC was delivered in eight, 90-minute sessions to parents; there was no child treatment component. Observed parent-therapist alliance recorded among 27 of the parents was measured using the Therapy Process Observational Coding System-Alliance scale (TPOCS-A; McLeod, 2005). Early alliance and change in alliance over time predicted improvements in several parenting behaviors and child outcomes, including peer sociometrics in a lab-based playgroup. These preliminary findings lend support to the importance of examining the parent-therapist alliance in parent-training groups for youth social and behavioral problems.

……..

Behav Ther. 2011 Jun;42:170-82.

CHANGES IN SELF-PERCEPTIONS IN CHILDREN WITH ADHD: A LONGITUDINAL STUDY OF DEPRESSIVE SYMPTOMS AND ATTRIBUTIONAL STYLE.

McQuade JD, Hoza B, Murray-Close D, et al.

This study examined positive self-perceptions in relation to depressive symptoms and attributional style in a sample of 88 boys with attention-deficit/hyperactivity disorder (ADHD) assessed at baseline and at a 2- to 3-year follow-up. Change in boys' self-perceptions of competency in the scholastic, social, and behavioral domains was examined as a predictor of changes in depressive symptoms and depressive attributional style. Additionally, teacher-rated perceptions of competency at baseline and follow-up were considered as unique predictors. Results indicated that across all three domains, a reduction in children's self-perceptions of competency over time predicted greater depressive symptoms at follow-up, even when controlling for teacher-rated competency. Analyses also suggested that a reduction in self-perceptions in the social domain was the strongest relative predictor of later depressive symptoms and also predicted greater depressive attributional style at follow-up. In contrast, teacher-rated competency was not a significant predictor of depressive symptoms or attributional style at follow-up. Results support a protective function of positive self-perceptions in regards to depressive cognitions over a 2- to 3-year period for children with ADHD. However, literature suggesting risks for other negative outcomes also is discussed.

……..

Behav Ther. 2011;42:462-74.

EFFECTIVENESS OF THE CHALLENGING HORIZONS AFTER-SCHOOL PROGRAM FOR YOUNG ADOLESCENTS WITH ADHD.

Evans SW, Schultz BK, DeMars CE, et al.

There are no empirically supported psychosocial treatments for adolescents with attention-deficit hyperactivity disorder (ADHD). This study examined the treatment benefits of the Challenging Horizons Program (CHP), a psychosocial treatment program designed to address the impairment and symptoms associated with this disorder in young adolescents. In addition to evaluating social and academic functioning outcomes, two critical questions from previous studies pertaining to the timing, duration, and family involvement in treatment were addressed. Forty-nine students recruited in two cohorts were randomly assigned to receive either the CHP or a community care condition. Outcomes suggested that students who received the CHP improved compared to students in the control condition on measures of symptoms and impairment. Implications related to timing, duration, and family involvement are reported, as well as recommendations for future studies.

……..

Behav Brain Funct. 2011;7.

THE 1287 G/A POLYMORPHISM OF THE NOREPINEPHRINE TRANSPORTER GENE (NET) IS INVOLVED IN COMMISSION ERRORS IN KOREAN CHILDREN WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER.

Song DH, Jhung K, Song J, et al.

Background: Previous evidence supports the role of noradrenergic systems in ADHD, and norepinephrine transporter (NET) is critical in regulating the noradrenergic system. The present study aimed to investigate the association between NET gene polymorphism and the performance measures of the Continuous Performance Test (CPT) in Korean ADHD children.

Methods: Eighty-seven children (mean age = 9.23 (plus or minus) 1.99 years) with ADHD were recruited from a university hospital. Genotypes of G1287A of the NET gene (SLC6A2) were analyzed. All participants completed the CPT, with performance measures of omission errors, commission errors, reaction time and reaction standardization computed. The relationship between G1287A polymorphisms and CPT performance measures was examined.

Results: There were 46 subjects with the G/G genotype, 35 subjects with the G/A genotype and 6 subjects with the A/A genotype. Among the three groups, there were no significant differences in the performance of CPTs. When dichotomized according to whether the subjects have the rare allele or not, subjects with the homozygous G/G genotype showed significantly lower commission errors compared to those without G/G genotypes (by independent T-test, $t = -2.18$, $p = 0.026$).

Discussion: Our study found a significant association between commission errors of the CPT and the G1287A genotype of the NET gene in Korean ADHD children. These findings suggest a protective role of the G/G genotype of the NET polymorphisms in the deficits of response inhibition in ADHD children.

……..

BMC Psychiatry. 2011;11.

CLINICAL SYMPTOMS AND PERFORMANCE ON THE CONTINUOUS PERFORMANCE TEST IN CHILDREN WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER BETWEEN SUBTYPES: A NATURAL FOLLOW-UP STUDY FOR 6 MONTHS.

Wang LJ, Huang YS, Chiang YL, et al.

Background: The aims of this study were to determine the time course of improvements in attention deficit hyperactivity disorder (ADHD) clinical symptoms and neurocognitive function in a realistic clinical setting, and the differences in ADHD symptom improvement using different classifications of ADHD subtypes.

Methods: The Child Behavior Checklist (CBCL) was completed by parents of ADHD children at the initial visit. The computerized Continuous Performance Test (CPT), Swanson, Nolan, and Pelham, and Version IV Scale for ADHD (SNAP-IV), and ADHD Rating Scale (ADHD-RS) were performed at baseline, one month, three months, and six months later, respectively. Patient care including drug therapy was performed

at the discretion of the psychiatrist. The ADHD patients were divided into DSM-IV subtypes (Inattentive, Hyperactive-impulsive and Combined type), and were additionally categorized into aggressive and non-aggressive subtypes by aggression scale in CBCL for comparisons.
Results: There were 50 ADHD patients with a mean age of 7.84 andplusmn; 1.64 years; 15 of them were inattentive type, 11 were hyperactive-impulsive type, and 24 were combined type. In addition, 28 of the ADHD patients were grouped into aggressive and 22 into non-aggressive subtypes. There were significant improvements in clinical symptoms of hyperactivity and inattention, and impulsivity performance in CPT during the 6-month treatment. The clinical hyperactive symptoms were significantly different between ADHD patients sub-grouping both by DSM-IV and aggression. Non-aggressive patients had significantly greater changes in distraction and impulsivity performances in CPT from baseline to month 6 than aggressive patients.
Conclusions: We found that ADHD symptoms, which included impulsive performances in CPT and clinical inattention and hyperactivity dimensions, had improved significantly over 6 months under pragmatic treatments. The non-aggressive ADHD patients might have a higher potential for improving in CPT performance than aggressive ones. However, it warrant further investigation whether the different classifications of ADHD patients could be valid for predicting the improvements in ADHD patients' clinical symptoms and neurocognitive performance.

……..

Brain. 2011;134:1740-50.

INDEPENDENT OSCILLATORY PATTERNS DETERMINE PERFORMANCE FLUCTUATIONS IN CHILDREN WITH ATTENTION DEFICIT/HYPERACTIVITY DISORDER.

Yordanova J, Albrecht B, Uebel H, et al.

The maintenance of stable goal-directed behaviour is a hallmark of conscious executive control in humans. Notably, both correct and error human actions may have a subconscious activation-based determination. One possible source of subconscious interference may be the default mode network that, in contrast to attentional network, manifests intrinsic oscillations at very low (<0.1 Hz) frequencies. In the present study, we analyse the time dynamics of performance accuracy to search for multisecond periodic fluctuations of error occurrence. Attentional lapses in attention deficit/hyperactivity disorder are proposed to originate from interferences from intrinsically oscillating networks. Identifying periodic error fluctuations with a frequency <0.1 Hz in patients with attention deficit/hyperactivity disorder would provide a behavioural evidence for such interferences. Performance was monitored during a visual flanker task in 92 children (7- to 16-year olds), 47 with attention deficit/hyperactivity disorder, combined type and 45 healthy controls. Using an original approach, the time distribution of error occurrence was analysed in the frequency and time-frequency domains in order to detect rhythmic periodicity. Major results demonstrate that in both patients and controls, error behaviour was characterized by multisecond rhythmic fluctuations with a period of ~12 s, appearing with a delay after transition to task. Only in attention deficit/hyperactivity disorder, was there an additional 'pathological' oscillation of error generation, which determined periodic drops of performance accuracy each 20-30 s. Thus, in patients, periodic error fluctuations were modulated by two independent oscillatory patterns. The findings demonstrate that: (i) attentive behaviour of children is determined by multisecond regularities; and (ii) a unique additional periodicity guides performance fluctuations in patients. These observations may re-conceptualize the understanding of attentive behaviour beyond the executive top-down control and may reveal new origins of psychopathological behaviours in attention deficit/hyperactivity disorder.

……..

Can J Psychiatry. 2011;56:281-92.

PSYCHIATRIC COMORBIDITIES IN ADOLESCENTS WITH ATTENTION-DEFICIT HYPERACTIVITY DISORDER AND THEIR SIBLINGS.

Yang LK, Shang CY, Gau SSF .

Objective: Despite high psychiatric comorbidities in adolescents with clinical diagnosis of attention-deficit hyperactivity disorder (ADHD), little is known about psychiatric comorbidities in their siblings. We investigated the psychiatric comorbid conditions in adolescents with ADHD, their siblings, and healthy control subjects from their school.

Method: The sample included 136 adolescent probands with ADHD according to the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV), diagnostic criteria; 136 siblings (47 affected and 89 unaffected) and 136 age- and sex-matched healthy school control subjects. All participants and their parents received the structured psychiatric interviews for current and lifetime DSM-IV psychiatric disorders of the participants.

Results: The rate of ADHD (34.6%) in the siblings of probands with ADHD was about 7 times higher than in the general population. Probands with ADHD were significantly more likely than unaffected siblings (OR 6.38; 95% CI 3.43 to 11.88) and healthy school control subjects (OR 9.60; 95% CI 5.31 to 17.34) to have a DSM-IV psychiatric disorder, including oppositional defiant disorder (ODD), conduct disorder (CD), tic disorders, major depressive disorder, specific phobia (more than control subjects only), nicotine use disorder, and sleep disorders. The affected siblings were significantly more likely than healthy school control subjects to have ODD, CD, specific phobia, and to have consumed alcohol (ORs ranging from 2.30 to 20.16).

Conclusions: Our findings suggest that siblings of probands with ADHD have increased risks for ADHD and that the affected siblings have more psychiatric comorbidities than healthy school control subjects. It warrants early identification of ADHD symptoms and other psychiatric comorbid conditions as well in siblings of adolescents with ADHD.

……..

Child Adolesc Psychiatry Ment Health. 2011;5.

ADHD PRESENTING AS RECURRENT EPISTAXIS: A CASE REPORT.

Rather YH, Sheikh AA, Sufi AR, et al.

Epistaxis is an important otorhinolaryngological emergency, which usually has an apparent etiology, frequently local trauma in children. Here we present a case report wherein the epistaxis was recalcitrant, and proved to have a psychiatric disorder as an underlying basis. The child was diagnosed with Attention Deficit/Hyperactivity Disorder, hyperactive type, which led to trauma to nasal mucosa due to frequent and uncontrolled nose picking. Treatment with atomoxetine controlled the patient's symptoms and led to a remission of epistaxis.

……..

Child Psychiatry Hum Dev. 2011 Jun;42:257-69.

ATOMOXETINE AND METHYLPHENIDATE TREATMENT IN CHILDREN WITH ADHD: THE EFFICACY, TOLERABILITY AND EFFECTS ON EXECUTIVE FUNCTIONS.

Yildiz O, Sismanlar SG, Memik NC, et al.

The aim of this study was to compare the safety, efficacy, tolerability, and the effects of atomoxetine and OROS-MPH on executive functions in children with ADHD. This study was an open-label study that only included two medication groups. Children were randomized to open-label atomoxetine or OROS-MPH for 12 weeks. Primary efficacy measures were T-DSM-IV-S, CGI-I and neuropsychological tests battery. Safety assessments included electrocardiogram, adverse events checklist and laboratory tests. According to the endpoint improvement scores of CGI and parents T-DSM-IV-S, treatment responses were not significantly different between the two study groups. OROS-MPH led to a significantly greater reduction in teacher T-DSM-IV-S scale scores. OROS-MPH was more effective than atomoxetine on Stroop-5 time and

number of corrections. Significant decrease in the percentage of perseverative errors on WCST in the OROS-MPH group was seen (p = 0.005). The most frequently reported adverse events in the atomoxetine group were anorexia, nausea, nervousness, weight loss, abdominal pain, and somnolence. In the OROS-MPH group, patients most frequently reported anorexia, nervousness, insomnia, headache, nausea, and weight loss. When all these results are considered, although both drugs can be considered effective in ADHD treatment, more remarkable improvement is provided by OROS-MPH based on the rates across informant (i.e., teachers, clinicians) and neuropsychological evaluation.

……..

Child Psychiatry Hum Dev. 2011 Jun;42:367-75.

ACETYL-L-CARNITINE AS AN ADJUNCTIVE THERAPY IN THE TREATMENT OF ATTENTION-DEFICIT/HYPERACTIVITY DISORDER IN CHILDREN AND ADOLESCENTS: A PLACEBO-CONTROLLED TRIAL.

Abbasi SH, Heidari S, Mohammadi MR, et al.

The objective of this study was to test whether a previous observed Acetyl-L-carnitine (ALC) treatment effect could be repeated in an ALC adjunctive therapy treatment trial of attention-deficit/hyperactivity disorder (ADHD) in children and adolescents. This was a six-week, randomized clinical trial undertaken in an outpatient child and adolescent clinic. Subjects included 40 outpatients (28 boys and 12 girls) between the ages of 7–13 who met the DSM-IV-TR diagnostic criteria for ADHD. All study subjects were randomly assigned to receive treatment using capsules of ALC doses ranging from 500 to 1,500 mg/day depending on the weight of the child plus methylphenidate at a dose of 20–30 mg/day depending on weight or Placebo plus methylphenidate at a dose of 20–30 mg/day depending on weight. The principal measure of outcome was the Teacher and Parent attention deficit/hyperactivity disorder Rating Scale- IV. No difference was observed between the two groups on the Parent and Teacher Rating Scale scores (df = 1; F = 0.10; P = 0.74 and df = 1; F = 0.22; P = 0.63 respectively). Side effects consisting of headache and irritability were observed more frequently in the methylphenidate plus placebo group. The results of this study do not support the application of ALC as an adjunctive therapy to methylphenidate in children and adolescents with ADHD.

……..

Chin J Contemp Pediatr. 2011;13:365-69.

EFFECTIVENESS AND SAFETY OF METHYLPHENIDATE AND ATOMOXETINE FOR ATTENTION DEFICIT HYPERACTIVITY DISORDER: A SYSTEMATIC REVIEW.

Lv XZ, Shu Z, Zhang YW, et al.

Objective: To assess and compare the effectiveness and safety of methylphenidate immediate-release tablets (IR-MPH), methylphenidate controlled release tablets (OROS-MPH) and atomoxetine (AHC) for attention deficit hyperactivity disorder (ADHD) in Chinese children.

Methods: Randomized or clinical controlled trials on the effectiveness and safety of IR-MPH, OROS-MPH and AHC for ADHD were searched in electronic databases of CNKI, VIP, CBMDISC online, PubMed, Embase and MEDLINE. Two reviewers independently extracted the data and assessed the quality of the included literatures.

Results: Eight trials were finally included. IR-MPH, OROS-MPH and AHC were effective for ADHD. OROS-MPH was superior to IR-MPH in the improvement of peer relationship, CGI-I score, mother satisfaction and psychosomatic problems. There were no significant differences in the effectiveness between the AHC and IR-MPH groups. The adverse events related to the therapy with IR-MPH, OROS-MPH or AHC were mild and the incidence rates of adverse events were not significantly different among the three groups.

Conclusions: The effectiveness of OROS-MPH for the treatment of ADHD is probably superior to IR-MPH, and the effectiveness between AHC and IR-MPH is similar. The three drugs demonstrate the safety and well tolerance.

……..

Clin Neuropharmacol. 2011;34:108-10.

METHYLPHENIDATE TREATMENT IN PEDIATRIC PATIENTS WITH ATTENTION-DEFICIT/ HYPERACTIVITY DISORDER AND COMORBID TRICHOTILLOMANIA: A PRELIMINARY REPORT.

Golubchik P, Sever J, Weizman A, et al.

Objectives: Trichotillomania (TTM) is a heterogenic mental disorder with a high rate of comorbidity and stressful life events (SLEs). Serotonergic and dopaminergic dysfunction are implicated in the pathophysiology of TTM. As in other impulse control disorders, increased prevalence of attention-deficit/ hyperactivity disorder (ADHD) is reported in patients with TTM as well. This study aimed to assess the efficacy and tolerability of methylphenidate (MPH) treatment in children and adolescents who met the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, criteria for both ADHD and TTM.

Methods: Nine children and adolescents, aged 6 to 18 years, diagnosed with ADHD and TTM, were treated with MPH for a 12-week period. The severity of ADHD was assessed using the ADHD Rating Scale, and the hair pulling was rated using the Massachusetts General Hospital Hair-Pulling Scale. Additional scales were used for assessing depression and anxiety levels, and history of SLE was recorded.

Results: Significant improvement was detected in ADHD after MPH treatment ($P < 0.003$), but no significant change was observed in hair pulling, as measured by the Massachusetts General Hospital Hair-Pulling Scale ($P = 0.096$) or in depression and anxiety levels. Lack of response of TTM to MPH (improvement, <50%) was associated with higher rate of positive SLE history ($P = 0.047$).

Conclusions: Some efficacy of MPH treatment was shown in TTM patients with low rate of SLE. A large-scale study is mandatory to evaluate the efficacy of MPH for TTM in ADHD/TTM patients.Trial Registration in www.clinicaltrials.gov.

……..

Clin Neurophysiol. 2011;122:1333-41.

BEHAVIOURAL DIFFERENCES BETWEEN EEG-DEFINED SUBGROUPS OF CHILDREN WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.

Clarke AR, Barry RJ, Dupuy FE, et al.

Objective: This study investigated the presence and nature of EEG clusters within a clinically-referred sample of children with Attention-Deficit/Hyperactivity Disorder (AD/HD), and whether behavioural differences exist between clusters.

Method: Participants were 155 boys with AD/HD and 109 age- and gender-matched controls. EEG was recorded during an eyes-closed resting condition and Fourier transformed to provide estimates for total power, and relative delta, theta, alpha, and beta. EEG data were grouped into 3 regions, and subjected to Cluster Analysis. Behavioural data for each cluster were compared against the remaining AD/HD subjects.

Results: Four EEG clusters were found. These were characterised by (a) elevated beta activity, (b) elevated theta with deficiencies of alpha and beta, (c) elevated slow wave with less fast wave activity, and (d) elevated alpha. An exploratory analysis of behavioural correlates with these EEG subtypes indicated the presence of interesting trends that need further investigation.

Conclusions: This study found that the AD/HD EEG profiles reported in past studies are robust and not substantially affected by the inclusion of children with other comorbid conditions. The observed group differences in behavioural profiles indicated that different patterns of EEG activity have importance in determining behaviour.

Significance: This is the first study to link behavioural profiles of children with AD/HD to specific EEG abnormalities.

……..

Clin Neurophysiol. 2011;122:1327-32.

EEG COHERENCE AND SYMPTOM PROFILES OF CHILDREN WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.

Barry RJ, Clarke AR, Hajos M, et al.

Objective: We compared EEG coherence in children with and without AD/HD, and sought to relate observed anomalies to AD/HD symptoms.

Methods: Forty children with AD/HD and 40 age- and sex-matched controls had eyes-closed resting EEG coherence calculated for eight interhemispheric electrode pairs and eight intrahemispheric pairs (four within each hemisphere) in the delta, theta, alpha, beta and "40 Hz" gamma bands.

Results: At short-medium inter-electrode distances, the AD/HD group had increased intrahemispheric coherence in delta and theta, and reduced (L. >. R) laterality in delta, alpha, beta and gamma. Over longer inter-electrode distances, the AD/HD group had reduced intrahemispheric coherence in alpha. In interhemispheric comparisons, the AD/HD group had reduced frontal coherence in delta, alpha and gamma, increased temporal theta and reduced temporal alpha coherences, and increased central/parietal/occipital coherence in theta. Smaller left-lateralized coherences in AD/HD correlated negatively with DSM Inattentive and DSM Total scores, and smaller frontal interhemispheric coherence in alpha correlated negatively with DSM Hyperactive/Impulsive score.

Conclusions: The negative correlations between AD/HD coherence anomalies and symptoms suggest that several anomalies reflect compensatory brain function.

Significance: Coherence differences in AD/HD may reflect anomalous frontal right-hemisphere linkages that help compensate functional brain anomalies in the left frontal regions in this disorder.

……..

Clin Psychol Rev. 2011 Jun;31:626-37.

NEUROPSYCHOLOGICAL BASIC DEFICITS IN PRESCHOOLERS AT RISK FOR ADHD: A META-ANALYSIS.

Pauli-Pott U, Becker K.

Widely accepted neuropsychological theories on attention deficit hyperactivity disorder (ADHD) assume that the complex symptoms of the disease arise from developmentally preceding neuropsychological basic deficits. These deficits in executive functions and delay aversion are presumed to emerge in the preschool period. The corresponding normative developmental processes include phases of relative stability and rapid change. These non-linear developmental processes might have implications for concurrent and predictive associations between basic deficits and ADHD symptoms. To derive a description of the nature and strength of these associations, a meta-analysis was conducted. It is assumed that weighted mean effect sizes differ between basic deficits and depend on age. The meta-analysis included 25 articles (n = 3005 children) in which associations between assessments of basic deficits (i.e. response inhibition, interference control, delay aversion, working memory, flexibility, and vigilance/arousal) in the preschool period and concurrent or subsequent ADHD symptoms or diagnosis of ADHD had been analyzed. For response inhibition and delay aversion, mean effect sizes were of medium to large magnitude while the mean effect size for working memory was small. Meta-regression analyses revealed that effect sizes of delay aversion tasks significantly decreased with increasing age while effect sizes of interference control tasks and Continuous Performance Tests (CPTs) significantly increased. Depending on the normative maturational course of each skill, time windows might exist that allow for a more or less valid assessment of a specific deficit. In future research these time windows might help to describe early developing forms of ADHD and to identify children at risk.

……..

CNS Drugs. 2011;25:503-09.

LOWER IQ IS ASSOCIATED WITH DECREASED CLINICAL RESPONSE TO ATOMOXETINE IN CHILDREN AND ADOLESCENTS WITH ATTENTION-DEFICIT HYPERACTIVITY DISORDER.

Mazzone L, Reale L, Mannino V, et al.

Objectives: Atomoxetine is commonly used to treat attention-deficit hyperactivity disorder (ADHD) in children with a broad range of cognitive abilities. We examined the association between level of cognitive functioning as determined by IQ and clinical response during treatment with atomoxetine.

Methods: The records of all the children and adolescents treated with atomoxetine at a university clinic in Catania, Italy, over a 3-year period were examined. A total of 55 clinically referred children and adolescents (aged 5-15 years, 53 males) with ADHD were treated with atomoxetine (10-110mg/day; mean: 1.28mg/kg/day) for a period ranging from 2 to 168 weeks (mean: 57.3 -SD 39.4, median: 56). The IQ was assessed as part of the diagnostic evaluation prior to starting treatment. During treatment, clinical outcome was rated on the Clinical Global Impression-Improvement (CGI-I) and CGI-Severity (CGI-S) scales.

Results: The IQ ranged from 43 to 117 (mean: 80.6 -SD 18.6, median: 84). The IQ and final CGI-I scores were negatively correlated (r=-0.68; p<0.01). Children and adolescents with an IQ <85 were less likely to be responders (defined as a final CGI-I score of 1 or 2) than children and adolescents with an IQ (double dagger)85 (20.71% vs 76.9%; p<0.001). None of the patients discontinued atomoxetine due to adverse effects, while treatment was discontinued in 20 subjects due to a lack of efficacy or ambivalence of parents about pharmacological treatment.

Conclusions: Atomoxetine appears to be less effective in children and adolescents with an IQ <85 than in children and adolescents in the average range of cognitive functioning. This difference is not accounted for by differences in the severity of ADHD symptoms, co-morbidity or reduced tolerability to the medication. These findings suggest that, in order to be fully informative, clinical trials of medications for ADHD should also include children and adolescents functioning in the borderline and cognitive disability range.

……..

Egypt J Neurol , Psychiatr Neurosurg. 2011;48:11-17.

AUTISTIC SPECTRUM DISORDERS AND HYPERACTIVITY IN EPILEPTIC CHILDREN.

Hussin RA, Ghani AAMA.

Background: It is well known that autistic disorders are associated with increased incidence of epilepsy, but very few studies investigate the incidence of autistic disorders and hyperactivity in epileptic patients.

Objective: Study of the autistic spectrum disorders and hyperactivity in epileptic children.

Methods: This study was carried out on 143 epileptic children, aged 2-15 years. They were subjected to complete neuropsychiatric examination, E.E.G. and examination for associated autistic disorder and hyperactivity through two stages study: in the first stage parents were asked to complete two scales, autism screening questionnaire and Rutter's parent questionnaire. In the second stage autism diagnostic interview revised was done.

Results: Of the 143 examined children, 23 cases (16%) were found to have autistic spectrum disorders. Children at risk of these disorders were found to have maternal and paternal ages more than 35 years, earlier onset of the first seizure, treated by more antiepileptic drugs, having more nocturnal seizures, more behavioral disorders, antisocial disorders and more hyperactivity symptoms than non autistic children.

Conclusion: This study suggests that children with epilepsy are at greater risk of having autistic spectrum and behavioral disorders, and so there is a need for more clinical vigilance to identify these disorders, as they could affect patients' quality of life and ability to learn.

……..

Epilepsy & Behavior. 2011 Mar;20:484-89.

ADHD AND EPILEPSY: CONTRIBUTIONS FROM THE USE OF BEHAVIORAL RATING SCALES TO INVESTIGATE PSYCHIATRIC COMORBIDITIES.

Loutfi KS, Carvalho AM, Lamounier JA, et al.

Children with epilepsy have a high incidence of psychiatric comorbidities, especially attention-deficit/hyperactivity disorder (ADHD). This observational cross-sectional study investigated the presence of ADHD in 30 children with idiopathic epilepsy. The Brazilian versions of the Child Behavior Checklist (CBCL), the Teacher Report Form (TRF), and the MTA-SNAP-IV questionnaire were used to assess comorbid psychiatric conditions. ADHD diagnosis was confirmed in 53.3% of children. The combined type was the most prevalent (43.7%), followed by the hyperactive–impulsive (37.5%) and inattentive (18.7%) types. Scores above the cutoff point on these scales were strongly correlated with the presence of ADHD. The high prevalence of ADHD in association with other psychiatric comorbidities in children with epilepsy justifies the use of behavioral rating scales as screening tests.

……..

Eur J Pharmacol. 2011;660:165-70.

Successful methylphenidate treatment of early onset extreme obesity in a child with a melanocortin-4 receptor gene mutation and attention deficit/hyperactivity disorder.

Albayrak O, Albrecht B, Scherag S, et al.

We present the case report of a 2 year old boy with early onset extreme obesity (body mass index (BMI) 34.2 kg/m2; body mass index standard deviation score (BMI-SDS) 5.4) who is heterozygous for a non-conservative functionally relevant melanocortin MC4 receptor mutation (Glu308Lys) and who also showed severe symptoms of attention deficit/hyperactivity disorder (ADHD). Treatment with the stimulant methylphenidate led to a sharp decrease of BMI to 21.8 kg/m2 (BMI-SDS 2.8) within 24 months. We discuss potential mechanisms for this unusually large weight loss and suggest a potential link between the melanocortinergic and the dopaminergic systems, and the sympathetic nervous system. The potential benefit of methylphenidate in obese melanocortin MC 4 receptor mutation carriers with and without co-morbid ADHD warrants further studies.

……..

Expert Rev Neurother. 2011 Apr;11:499-508.

TRANSITIONING TO OROS[SUP]®[/SUP] METHYLPHENIDATE FROM ATOMOXETINE IS EFFECTIVE IN CHILDREN AND ADOLESCENTS WITH ADHD.

Niederkirchner K, Slawik L, Wermelskirchen D, et al.

Objective: To explore the clinical outcomes of children/adolescents with attention-deficit/hyperactivity disorder (ADHD) who required a therapy switch from atomoxetine to OROS® methylphenidate (MPH).

Methods : This prospective, noninterventional study involved patients aged 6-18 years with a confirmed diagnosis of ADHD who experienced insufficient clinical response and/or poor tolerability during atomoxetine treatment. Patients were transitioned to OROS MPH and followed for 12 weeks. ADHD symptoms, functional outcomes, health-related quality of life (HRQoL) and tolerability were assessed throughout the study.

Results: 42 patients (intention-to-treat) transitioned from atomoxetine 43.2 plus 14.7 mg onto OROS MPH 33.0 plus 17.7 mg (mean daily starting dose), increasing to 38.6 plus 17.6 mg at the final visit. Median treatment duration was 85 days (range: 3-155). Compared with baseline, symptoms, functional outcome and HRQoL improved after transitioning to OROS MPH as assessed by the Conners' Parent Rating Scale (mean change from baseline: -10.1 ± 11.6; $p < 0.0001$), Children's Global Assessment Scale (8.7 ± 16.2; $p = 0.0015$) and ILC-LQO-28 scores (parents' rating from 14.9 ± 3.6 [baseline] to 17.5 ± 4.8 [study end]; $p = 0.0002$; patients' rating from 16.9 ± 3.9 [baseline] to 19.3 ± 4.4 [study end]; $p = 0.0003$). Social interactions and late afternoon tasks (playing with other children, household chores, school homework and behavior

towards visitors/at visits) improved ($p < 0.001$). Approximately 62% expressed satisfaction ('very good' or 'good') with OROS MPH therapy compared with prior atomoxetine with respect to symptom control in the late afternoon. The most common treatment-emergent adverse events after switching were involuntary muscle contractions (tics; 16.7%), insomnia (14.3%), abdominal pain (9.5%) and headache (9.5%). No clinically relevant changes in body weight or vital signs were observed.
Conclusion: In this naturalistic setting, transitioning from atomoxetine to OROS MPH was associated with improved ADHD symptoms and impacted positively on patients' and parents' HRQoL and disease burden in ADHD children who demonstrated an insufficient response and/or poor tolerability to atomoxetine.

……..

Future Neurol. 2011;6:399-413.
CHILD AND CAREGIVER ISSUES IN THE TREATMENT OF ATTENTION DEFICIT-HYPERACTIVITY DISORDER: EDUCATION, ADHERENCE AND TREATMENT CHOICE.
Ferrin M, Taylor E.
There is much more to successful drug treatment than writing a prescription. In this article, we describe some of the 'holistic' aspects of the pharmacological treatment of attention deficit-hyperactivity disorder, with an emphasis on helping families to decide between psychological and pharmacological treatment and on the process of psychoeducation. Detailed accounts of drug and behavioral treatment in various circumstances are available elsewhere; however, the value and process of psychoeducation is sometimes underestimated or referred to in a cursory statement of the need for a good doctor-patient relationship. There has been little in the way of controlled trials, so no meta-analysis is attempted. Where possible (e.g., in reviewing the effects of psychological therapy and prediction of drug response), PubMed/Medline was searched for systematic reviews and randomized trials, but this article's conclusions should be taken as personal. These subjective views are based chiefly on experience in clinical practice, participation in focus groups with young people and their families and work with support groups.

……..

Hum Psychopharmacol. 2011;26:155-60.
DULOXETINE IN THE TREATMENT OF ADOLESCENTS WITH ATTENTION DEFICIT/HYPERACTIVITY DISORDER: AN OPEN-LABEL STUDY.
Mahmoudi-Gharaei J, Dodangi N, Tehrani-Doost M, et al.
Objective The main aim of this study was to explore the efficacy and safety of duloxetine, a serotonin and norepinephrine reuptake inhibitor, in the treatment of adolescents with attention deficit/hyperactivity disorder (ADHD).
Methods Seventeen adolescents aged 11-18years, diagnosed with ADHD, participated in this 6-week open-label study. Duloxetine was given in doses of 30mg/day in the first week and 60mg/day from week2 to the end of the study. Conners' Parent Rating Scale-Revised (CPRS-R) short form was used to assess the efficacy of the therapy.
Results A significant reduction in ADHD symptoms measured by CPRS-R was observed. This reduction was evident from week4 of the study. In addition, the decrease was significant in all four subscales of CPRS-R including inattention, oppositionality, hyperactivity and ADHD index. In terms of side effects, duloxetine was generally safe and well tolerated.
Conclusions The results of this open-label study suggest a promise of duloxetine in the treatment of youth with ADHD. Further controlled studies with larger samples are required to evaluate the efficacy of duloxetine in children and adolescents with ADHD.

……..

Indian Journal of Community Psychology. 2011 Mar;7:12-19.

EXECUTIVE FUNCTIONS OF CHILDREN WITH LEARNING PROBLEMS.

Visalakshi N, Thenmozhi S.

This study investigates the multiple aspects of executive functioning in children with and without learning disabilities and ADHD and children with learning disabilities. 16 children with LD, 16 children without LD and ADHD and 16 children with ADHD comorbid with LD participated in the study. A battery of neuropsychological tests was utilized to evaluate deficits in selective attention, sustained attention, switching attention, verbal fluency, category fluency, design fluency, response inhibition and working memory. Participants were unmedicated at the time of testing, were administered three tests of executive function and attention (letter cancellation, digit vigilance, triads task, controlled oral word association, animal name test, design fluency, go/no go test, stop signal test, Stroop colour word test, N back test—verbal and visual). Statistical analysis was done (t test, correlation,).Results indicate that there is significant difference in the executive functions between children with LD, children with LD-ADHD and children without LD and ADHD. There is no significant difference in the executive functions between children with LD and children with LD-ADHD. Children with LD have better interference control than children with LD-ADHD, which might be because of the presence of ADHD behaviour.

……..

Int J Obes. 2011;35:852-62.

ASSOCIATION BETWEEN ATTENTION-DEFICIT/HYPERACTIVITY DISORDER SYMPTOMS AND OBESITY AND HYPERTENSION IN EARLY ADULTHOOD: A POPULATION-BASED STUDY.

Fuemmeler BF, Ostbye T, Yang C, et al.

Objective: To examine the associations between attention-deficit/ hyperactivity disorder (ADHD) symptoms, obesity and hypertension in young adults in a large population-based cohort.

Design, Setting and Participants: The study population consisted of 15 197 respondents from the National Longitudinal Study of Adolescent Health, a nationally representative sample of adolescents followed from 1995 to 2009 in the United States. Multinomial logistic and logistic models examined the odds of overweight, obesity and hypertension in adulthood in relation to retrospectively reported ADHD symptoms. Latent curve modeling was used to assess the association between symptoms and naturally occurring changes in body mass index (BMI) from adolescence to adulthood.

Results: Linear association was identified between the number of inattentive (IN) and hyperactive/impulsive (HI) symptoms and waist circumference, BMI, diastolic blood pressure and systolic blood pressure (all P-values for trend 0.05). Controlling for demographic variables, physical activity, alcohol use, smoking and depressive symptoms, those with three or more HI or IN symptoms had the highest odds of obesity (HI 3, odds ratio (OR)1.50, 95% confidence interval (CI)1.222.83; IN 3, OR1.21, 95% CI1.021.44) compared with those with no HI or IN symptoms. HI symptoms at the 3 level were significantly associated with a higher OR of hypertension (HI 3, OR1.24, 95% CI1.011.51; HI continuous, OR1.04, 95% CI1.001.09), but associations were nonsignificant when models were adjusted for BMI. Latent growth modeling results indicated that compared with those reporting no HI or IN symptoms, those reporting 3 or more symptoms had higher initial levels of BMI during adolescence. Only HI symptoms were associated with change in BMI.

Conclusion: Self-reported ADHD symptoms were associated with adult BMI and change in BMI from adolescence to adulthood, providing further evidence of a link between ADHD symptoms and obesity.

……..

Int J Psychophysiol. 2011;81:1-11.

INHIBITION CONTROL AND ERROR PROCESSING IN CHILDREN WITH ATTENTION DEFICIT/HYPERACTIVITY DISORDER: AN EVENT-RELATED POTENTIALS STUDY.

Shen IH, Tsai SY, Duann JR.

We studied inhibitory control and error processing in a task requiring inhibition of a motor response. Behavioral and ERP indices were recorded in fourteen ADHD and fourteen healthy children aged between 6 and 10. years during the Stop signal task (SST). The ADHD group made more variable in RT and showed less accuracy, more omissions and choice errors. Also, the ADHD group had a tendency toward a lower probability of inhibition and a longer Stop signal reaction time. The ADHD group also displayed a flatter response inhibition slope compared to the control group. Smaller P1 in ADHD group reflected that the ADHD group has less efficient attention than the control group. Furthermore, the ADHD group showed normal ERN, reduced Pe (retrieved from response-locked epochs), and reduced LPW (retrieved from Stop signal-locked epochs), suggesting that they might be normal in early error monitoring process related to error detection, but show abnormal in later error monitoring process associated with a conscious evaluation of the error. Behavioral and ERP data of the present study show deficient selective attention, inhibitory control, and error processing in children of ADHD.

……..

J Am Acad Child Adolesc Psychiatry. 1988 Nov;27:802-05.

THE ACTION OF STIMULANT MEDICATION IN ATTENTION DEFICIT DISORDER WITH HYPERACTIVITY: DOPAMINERGIC, NORADRENERGIC, OR BOTH?

Levy F, Hobbes G.

……..

JCRPE J Clin Res Pediatr Endocrinol. 2011;3:95-97.

CASE REPORT: TWO PATIENTS WITH PARTIAL DIGEORGE SYNDROME PRESENTING WITH ATTENTION DISORDER AND LEARNING DIFFICULTIES.

Hacihamdioglu B, Berberoglu M, Siklar Z, et al.

DiGeorge syndrome (DGS) has classically been characterized by the triad of clinical features including congenital cardiac defects, immune deficiencies secondary to aplasia or hypoplasia of the thymus, and hypocalcaemia due to small or absent parathyroid glands. The phenotypic features of these patients are much more variable and extensive than previously recognized. The acknowledgement of similarities and phenotypic overlap of DGS with other disorders associated with genetic defects in 22q11 has led to an expanded description of the phenotypic features of DGS including palatal/speech abnormalities, as well as cognitive, neurological and psychiatric disorders. Here, we report the cases of two DGS patients with dysmorphic facial features who were initially admitted to the Psychiatry Department for attention disorder and learning difficulties.

……..

J Adolesc. 2011 Jun;34:485-92.

ADOLESCENTS' BELIEFS ABOUT SOURCES OF HELP FOR ADHD AND DEPRESSION.

Swords L, Hennessy E, Heary C.

The peer group begins to become a source of support during late childhood and adolescence making it important to understand what type of help young people might suggest to a friend with an emotional or behavioral problem. Three groups of young people participated in the study with average ages of 12 (N = 107), 14 (N = 153) and 16 years (N = 133). All participants were presented with vignettes describing fictional peers, two of whom had symptoms of clinical problems (ADHD and depression) and a third comparison peer without symptoms. Results indicate that all participants distinguished between clinical and

comparison vignette characters and they believed that the characters with clinical symptoms needed help. The 16-year-olds were more likely to differentiate between the two clinical vignettes in terms of the type of help suggested. The results are discussed in light of previous research on adolescents' understanding of sources of help for mental health problems.

……..

J Child Adolesc Psychopharmacol. 2011;21:255-63.

PHARMACOKINETICS AND THERAPEUTIC EFFECT OF OROS(REGISTERED TRADEMARK) METHYLPHENIDATE UNDER DIFFERENT BREAKFAST CONDITIONS IN CHILDREN WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.

Wigal SB, Gupta S, Heverin E, et al.

Objective: To examine the pharmacokinetics (PKs) and pharmacodynamics (PDs) of OROS(registered trademark) methylphenidate (OROS MPH) dosed once daily (QD) versus an early standard regimen (immediate-release [IR] MPH dosed three times daily [TID]) under various breakfast conditions.

Methods: This single-center, double-blind, double-dummy, randomized, crossover study of OROS MPH (NCT00269815) in children aged 6 to 12 years with attention-deficit/ hyperactivity disorder evaluated the PKs and PDs of MPH given with different breakfast conditions: OROS MPH administered after a high-fat breakfast, after a normal breakfast, or after fasting and IR MPH administered after a normal breakfast or after fasting in the morning and at two subsequent time points during the day. To maximize information, patients were divided into two groups, each receiving three of the five treatments for 1 day in a three-period, randomized, crossover design. Patients were assigned to 1 of 3 dosage levels (OROS MPH 18, 36, and 54 mg QD, and an assumed equivalent regimen of IR MPH 5, 10, and 15 mg given TID) based on their prestudy established clinical dose of IR MPH. PD measurements included Combined-Attention and Deportment scores on a rating scale of school behavior (the Swanson, Kotkin, Agler, M-Flynn, and Pelham), global assessments of efficacy, and activity monitor levels during academic seatwork. Serial blood samples for PK analysis were taken predose, and then every 60 to 90 minutes until 11.5 hours postdose. Vital signs were assessed predose, and then every 1.5 to 2.5 hours until 11.5 hours postdose.

Results: Of the 32 patients enrolled, 31 completed the study. The PK profiles for MPH after OROS MPH administration were similar under all conditions (with normal, high-fat breakfast, or fasting). No bioequivalence tests of OROS MPH and IR MPH under various breakfast conditions were done because there were so few patients in each dose level of treatment. The two IR MPH conditions (after normal breakfast and fasting) were not compared. The drug-to-metabolite ratios (area under the curve) for all OROS MPH and IR MPH treatments were similar. OROS MPH and IR MPH provided a similar therapeutic effect, irrespective of breakfast conditions, as demonstrated by the Swanson, Kotkin, Agler, M-Flynn, and Pelham Attention and Deportment measures and global assessments. No serious adverse events, no deaths, and no clinically significant changes in vital signs were reported, except for one patient who was discontinued early because of repeated systolic blood pressure elevations on study day 1.

Conclusions: The results of this study demonstrate that in children with attention-deficit/hyperactivity disorder, administering OROS MPH with or without food produces similar PK and PD profiles.

……..

J Child Adolesc Psychopharmacol. 2011;21:265-73.

Differential effects of predictors on methylphenidate initiation and discontinuation among young people with newly diagnosed attention-deficit/ hyperactivity disorder.

Chen CY, Yeh HH, Chen KH, et al.

Objective: Previous population-based studies have identified factors accounting for differential utilization of psychotropic medications among young patients with attention-deficit/hyperactivity disorders (ADHDs); yet, few analyses have addressed changes in such factors that can occur in the help-seeking process. The aim of this study was to examine patient- and service provider-level predictors for methylphenidate (MPH) initiation and discontinuation.

Method: This cohort study included 10,153 newly diagnosed ADHD patients under 18 years of age in 2000, identified from the National Health Insurance Research Database. The risk association was estimated by time-dependent survival analyses, as indexed by hazard ratio.
Results: Approximately 30% of young people received MPH treatment within the year of their ADHD diagnosis, and virtually none remained in treatment beyond 12 months. Regardless of co-morbidity status, the following were significantly associated with earlier initiation of MPH treatment: older age (e.g., adjusted hazard ratio [aHR] for age 12-17 = 4.5-7.6), lower socioeconomic status (aHR = 1.2-1.4), southern residence (aHR = 1.4-1.6), receiving the diagnosis while school was in session (aHR = 1.3-1.4), receiving the diagnosis from a physician specializing in pediatrics or psychiatry (aHR = 7.3-16.8), and receiving the diagnosis in a district hospital/clinic (aHR = 1.3-1.7). However, once treatment started, older ages appeared to increase the risk of early discontinuation by 15%, and the corresponding estimates for receiving initial MPH in a regional hospital or district hospital/clinic were 27% and 32%, respectively. Change in treatment location upon subsequent visit was associated with a 58% reduction in early discontinuation.
Conclusions: This information about time-varying predictors for MPH utilization throughout treatment may provide insight into the delivery of pediatric mental health services and has important implications for the design of clinical treatment programs.

……..

J Child Adolesc Psychopharmacol. 2011;21:245-53.

EFFECTS OF METHYLPHENIDATE ON INTELLIGENCE AND ATTENTION COMPONENTS IN BOYS WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.

Hellwig-Brida S, Daseking M, Keller F, et al.

Background: Methylphenidate (MPH) is an efficient treatment to reduce behavioral symptoms of attention-deficit/hyperactivity disorder (ADHD); however, its impact on cognitive functioning has not been sufficiently demonstrated so far. This study investigates the hypothesis that MPH improves attention-related cognitive functions.
Methods: Sixty-seven medication-naive boys aged 6-13, with newly diagnosed ADHD, were tested before treatment with a neuropsychological assessment battery, including the Wechsler Intelligence Scales for Children (WISC-IV) and the Test of Attentional Performance for Children (KITAP). A follow-up assessment was performed after 8-12 weeks, with 37 participants receiving MPH treatment and 30 controls without medication. The effect of MPH on test performance was analyzed by repeated measures analyses of variance.
Results: Both groups improved significantly across a broad range of psychometric measures of cognitive performance. There were no significant interaction effects of group and time on attention-related cognitive functions. Exploratory analyses revealed an effect of MPH on verbal comprehension in the WISC-IV.
Conclusion: The study results do not support that MPH improves attention-related cognitive functions of boys with ADHD. The potential effect of MPH on verbal abilities deserves further research.

……..

Journal of Child Psychology and Psychiatry. 2011 May;52:547-57.

A MULTIPLE DEFICIT MODEL OF READING DISABILITY AND ATTENTION-DEFICIT/HYPERACTIVITY DISORDER: SEARCHING FOR SHARED COGNITIVE DEFICITS.

McGrath LM, Pennington BF, Shanahan MA, et al.

Background: This study tests a multiple cognitive deficit model of reading disability (RD), attention-deficit/hyperactivity disorder (ADHD), and their comorbidity.
Methods: A structural equation model (SEM) of multiple cognitive risk factors and symptom outcome variables was constructed. The model included phonological awareness as a unique predictor of RD and response inhibition as a unique predictor of ADHD. Processing speed, naming speed, and verbal working memory were modeled as potential shared cognitive deficits.

Results: Model fit indices from the SEM indicated satisfactory fit. Closer inspection of the path weights revealed that processing speed was the only cognitive variable with significant unique relationships to RD and ADHD dimensions, particularly inattention. Moreover, the significant correlation between reading and inattention was reduced to non-significance when processing speed was included in the model, suggesting that processing speed primarily accounted for the phenotypic correlation (or comorbidity) between reading and inattention.
Conclusions: This study illustrates the power of a multiple deficit approach to complex developmental disorders and psycho-pathologies, particularly for exploring comorbidities. The theoretical role of processing speed in the developmental pathways of RD and ADHD and directions for future research are discussed.

……..

J Intellect Disabil Res. 2011;55:623-35.

ATTENTION-DEFICIT/HYPERACTIVITY DISORDER AMONG CHILDREN WITH AND WITHOUT INTELLECTUAL DISABILITY: AN EXAMINATION ACROSS TIME.

Neece CL, Baker BL, Blacher J, et al.

Background Children with intellectual and developmental disabilities are at heightened risk for mental disorders, and disruptive behaviour disorders appear to be the most prevalent. The current study is a longitudinal examination of attention-deficit/hyperactivity disorder (ADHD) among children with and without intellectual disability (ID) across ages 5 to 8.
Method We assessed 228 5-year-old children, 87 with ID and 141 with typical development (TD), for clinical diagnoses using a structured interview. These interviews were conducted with mothers annually from child age 5 to 8.
Results Attention-deficit/hyperactivity disorder was over 3 times as prevalent in the ID group as in the TD group across ages 5, 6, 7 and 8. The diagnosis of ADHD tended to emerge earlier and was more stable in the ID group; however, the total number and relative frequency of ADHD symptoms endorsed appeared to be similar within the two groups across time. With respect to the developmental course, the trajectories of ADHD inattentive and hyperactive/impulsive symptoms over time were similar in the two groups.
Discussion Children with ID appear to be at heightened risk for ADHD and they may experience a longer and more persistent course of the disorder. These findings highlight the need for making interventions available for early treatment of this condition in children with ID.

……..

Journal of Research in Special Educational Needs. 2011 Mar;11:20-29.

HOME–SCHOOL PARTNERSHIP AND THE CONSTRUCTION OF DEVIANCE: BEING AND BECOMING THE GOLDFISH FAMILY.

Watson C.

Partnership between home and school is a key aspect of current educational policy. At the level of policy of the notion of partnership is constructed unproblematically as smooth consensus, but this may not be the way it plays out in school where deeply rooted assumptions surrounding parenthood—and in particular motherhood—may pertain. This paper is concerned with home–school relations and the way in which schools construct deviance and attribute stigma. It is an analysis of a narrative written by a parent of a child diagnosed with attention deficit hyperactivity disorder. It explores Jenny's narrative concerning the events surrounding the diagnosis, in particular the part played by the school in this process, and the descent of a family from normality into madness. The paper begins with the attribution of deviance, the development of stigma and the birth of the Goldfish family. It then goes on to present three Hogarthian scenes documenting the family's progress, and examines the peculiar convergence of social pressures which result in madness, before drawing some conclusions concerning the construction of deviance and the role of the school in this.

……..

J Am Acad Child Adolesc Psychiatry. 2011;50:593-601.

NEUROANATOMICAL AND NEUROPSYCHOLOGICAL CORRELATES OF THE CEREBELLUM IN CHILDREN WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER-COMBINED TYPE.

Bledsoe JC, Semrud-Clikeman M, Pliszka SR.

Objective: Studies of healthy individuals and those with cerebellar damage have implicated the cerebellum in a variety of cognitive and behavioral processes. Decreased cerebellar volume has been found in children with attention-deficit/hyperactivity disorder (ADHD) and differentially related to behavioral outcomes. The present study investigated whether smaller cerebellar vermis volume was present in children with ADHD-combined type (ADHD-C) compared with controls and whether volume related to parent- and teacher-reported levels of ADHD symptomatology.

Method: T1-weighted magnetic resonance images and parent- and teacher-reported ADHD symptoms were acquired for 32 children diagnosed with ADHD-C and 15 typically developing controls. Participants were right-handed, had no comorbid diagnoses of learning disabilities, conduct disorder, or affective/mood disorder, and were 9 to 15 years of age.

Results: Participants with ADHD-C showed significantly smaller volume in the posterior inferior vermis compared with controls. No statistically significant differences were observed for cerebral volume, anterior vermis volume, posterior superior volume, or total cerebellar volume. Regression analyses indicated that a significant amount of the variance in parent-reported Behavior Assessment System for Children, Second Edition, Hyperactivity and Attention and Conners Restless/Impulsive ratings was explained by volume of the posterior inferior vermis.

Conclusions: Consistent with previous studies, children with ADHD had smaller volume in the posterior inferior vermis. New findings emerged with smaller volume of the posterior inferior vermis predicting a significant amount of the variance in parent-reported hyperactivity, attention, and restlessness/impulsivity. Thus, symptoms of hyperactivity and inattention in ADHD may be partly explained by smaller volume of the cerebellar vermis and its connections within the cerebrum.

……..

J Am Acad Child Adolesc Psychiatry. 2011;50:554-62.

SHORT-TERM PERSISTENCE OF DSM-IV ADHD DIAGNOSES: INFLUENCE OF CONTEXT, AGE, AND GENDER.

Bauermeister JJ, Bird HR, Shrout PE, et al.

Objective: Little is known about the effect of social context and gender on persistence of attention-deficit/hyperactivity disorder (ADHD) in children of early and middle school years. The study compared persistence of DSM-IV ADHD and ADHD not otherwise specified (NOS) over 2 years in two groups of Puerto Rican children.

Method: A three-wave study obtained data on Puerto Rican children 5 through 13 years of age at baseline. Samples were drawn in the South Bronx in New York (n = 1,138) and two metropolitan areas in Puerto Rico (n = 1,353). The Diagnostic Interview Schedule for Children Version IV was used to diagnose ADHD and ADHD-NOS.

Results: ADHD or ADHD-NOS diagnosis at wave 1 strongly predicted disorder at waves 2 and 3. ADHD had a significantly stronger predictive effect than ADHD-NOS consistently across site and gender. There was a significant interaction with baseline age. For those younger at baseline, the strength of the prediction of ADHD-NOS was relatively weak; for older children, the presence of ADHD-NOS at baseline predicted risk of subsequent ADHD or ADHD-NOS.

Conclusions: Persistence of ADHD in children of similar ethnicity does not manifest differently across context and gender. Results suggest that age-specific symptom criteria and modification of age-of-onset criteria should be considered for the diagnosis.

……..

J Am Acad Child Adolesc Psychiatry. 2011;50:543-53.

DOES ADHD PREDICT SUBSTANCE-USE DISORDERS? A 10-YEAR FOLLOW-UP STUDY OF YOUNG ADULTS WITH ADHD.

Wilens TE, Martelon M, Joshi G, et al.

Objective: High rates of substance-use disorders (SUD) have been found in samples of adolescents and adults with attention-deficit/hyperactivity disorder (ADHD). Predictors of SUD in children with ADHD who are at risk for the development of SUDs remain understudied. The main aims of this study were to identify clinically meaningful characteristics of children that predicted the future development of SUDs and to see whether the role of these characteristics varied by sex.

Method: Subjects were children and adolescents with (n = 268; mean age (plus or minus) standard deviation = 10.9 (plus or minus) 3.2 years) and without (n = 229; mean age 11.9 (plus or minus) 3.3 years) DSM-III-R ADHD followed prospectively and blindly over a 10-year follow-up period onto young adult years. Subjects were assessed with structured diagnostic interviews for psychopathology and SUDs.

Results: Over the 10-year follow-up period, ADHD was found to be a significant predictor of any SUD (hazards ratio 1.47; 95% confidence interval 1.072.02; p = .01) and cigarette smoking (2.38; 1.613.53; p < .01). Within ADHD, comorbid conduct disorder (2.74; 1.664.52; p < .01) and oppositional defiant disorder (2.21; 1.403.51; p < .01) at baseline were also found to be significant predictors of SUDs. Similar results were found for cigarette-, alcohol-, and drug-use disorders. There were few meaningful sex interaction effects. No clinically significant associations were found for any social or family environment factors or for cognitive functioning factors (p > .05 for all comparisons).

Conclusions: These results indicate that ADHD is a significant risk factor for the development of SUDs and cigarette smoking in both sexes.

……..

J Neurol Sci. 2011.

DEVELOPMENTAL ASPECTS OF ENVIRONMENTAL NEUROTOXICOLOGY: LESSONS FROM LEAD AND POLYCHLORINATED BIPHENYLS.

Winneke G.

The particular vulnerability of the developing nervous system for low-level exposure to chemicals is well established. It has been argued that some degree of developmental neurotoxicity was found for a large number of industrial chemicals. However, for only few of these, namely inorganic lead, arsenic, organic mercury and polychlorinated biphenyls (PCBs), human evidence is available to suggest that these may cause neurodevelopmental adversity and may, thus, be involved in contributing to neurodevelopmental disorders like autism, attention-deficit disorder, mental retardation or cerebral palsy. The focus of this overview is on PCBs and inorganic lead as developmental neurotoxicants at environmental levels of exposure. The adverse effects of inorganic lead on the developing brain have long been studied, and much emphasis has been on subtle degrees of mental retardation in terms of intelligence (IQ). The evidence is consistent, but the effect sizes are typically small. Research interest has also been devoted to studying aspects of "attention-deficit hyperactivity disorder" (ADHD) in children in relation to environmental exposure to lead in both cross-sectional and case-control studies. More recently, we have also studied core elements of ADHD according to ICD-10 and DSM-IV in relation to environmental exposure to lead, mercury and aluminum in asymptomatic school children in Romania. Both, performance measures (several attention tasks) and questionnaire-based behavior ratings from parents and teachers showed that lead, but not Hg or Al, was consistently and adversely associated with core elements of ADHD. These findings in asymptomatic children nicely fit into the overall pattern of observations and suggest that, apart from genetic influences, low-level exposure to lead contributes to this neurodevelopmental disorder. Polychlorinated biphenyls (PCBs) are persistent organic pollutants with lipophilic properties. Due to their persistence, they are still present in environmental media at potentially harmful concentrations, although production and use of PCBs was already banned in the early 1980s. Several prospective cohort studies-including our Dusseldorf study-have demonstrated that pre- and early postnatal exposure to PCBs is associated with deficit or retardation of mental and/or motor development, even after adjusting for maternal intelligence and developmental effects of the quality of the home environment. The pathophysiology is still unclear, although

interference with thyroid metabolism during brain development is being discussed. Based on these reviews, three aspects, namely pre- vs. postnatal impact, effect scaling for comparative purposes, and integration of neurobehavioral findings into clinical and neuroscience contexts, are outlined as lessons learned from neurodevelopmental observations in children environmentally exposed to lead or PCBs.

……..

NeuroImage. 2011;56:2209-17.

IMPAIRED ATTENTION AND NETWORK CONNECTIVITY IN CHILDHOOD ABSENCE EPILEPSY.

Killory BD, Bai X, Negishi M, et al.

Patients with childhood absence epilepsy (CAE) often demonstrate impaired interictal attention, even with control of their seizures. No previous study has investigated the brain networks involved in this impairment. We used the continuous performance task (CPT) of attentional vigilance and the repetitive tapping task (RTT), a control motor task, to examine interictal attention in 26 children with CAE and 22 matched healthy controls. Each subject underwent simultaneous 3. T functional magnetic resonance imaging-electroencephalography (fMRI-EEG) and CPT/RTT testing. Areas of activation on fMRI during the CPT task were correlated with behavioral performance and used as seed regions for resting functional connectivity analysis. All behavioral measures reflecting inattention were significantly higher in patients. Correlation analysis revealed that impairment on all measures of inattention on the CPT task was associated with decreased medial frontal cortex (MFC) activation during CPT. In addition, analysis of resting functional connectivity revealed an overall decrease within an 'attention network' in patients relative to controls. Patients demonstrated significantly impaired connectivity between the right anterior insula/frontal operculum (In/FO) and MFC relative to controls. Our results suggest that there is impaired function in an attention network comprising anterior In/FO and MFC in patients with CAE. These findings provide an anatomical and functional basis for impaired interictal attention in CAE, which may allow the development of improved treatments targeted at these networks.

……..

Neuropsychologia. 2011;49:1641-50.

FMRI ACTIVATION DURING RESPONSE INHIBITION AND ERROR PROCESSING: THE ROLE OF THE DAT1 GENE IN TYPICALLY DEVELOPING ADOLESCENTS AND THOSE DIAGNOSED WITH ADHD.

Braet W, Johnson KA, Tobin CT, et al.

The DAT1 gene codes for the dopamine transporter, which clears dopamine from the synaptic cleft, and a variant of this gene has previously been associated with compromised response inhibition in both healthy and clinical populations. This variant has also been associated with ADHD, a disorder that is characterised by disturbed dopamine function as well as problems with response inhibition. In the present study we used fMRI to investigate the role of dopaminergic genetic variation on executive functioning by comparing how activation associated with successful and unsuccessful inhibitions differs based on DAT1-genotype and ADHD-diagnosis in adolescents performing a go/nogo task. The results identify regional specificity concerning which functional differences can be attributed to the possession of the high risk DAT1 genotype, the clinical condition or an interaction between the two. During response inhibition, individuals with two copies of the 10-repeat allele showed increased activation in frontal, medial, and parietal regions, which may indicate that inhibition is more effortful for this group. Conversely, this group displayed a reduced error response in the parahippocampal gyrus, suggestive of reduced learning from errors. There were also a number of frontal, parietal, medial and occipital regions, where the relationship between genotype and fMRI-activation differed between the ADHD group and the typically developing adolescents. Finally, the ADHD group displayed decreased activation in parietal and (pre)frontal regions during response inhibition, and in frontal and medial brain regions on error trials.

……..

Neuropsychopharmacology. 2011;36:1575-86.

METHYLPHENIDATE NORMALIZES FRONTO-STRIATAL UNDERACTIVATION DURING INTERFERENCE INHIBITION IN MEDICATION-NAVE BOYS WITH ATTENTION-DEFICIT HYPERACTIVITY DISORDER.

Rubia K, Halari R, Cubillo A, et al.

Youth with attention deficit hyperactivity disorder (ADHD) have deficits in interference inhibition, which can be improved with the indirect catecholamine agonist methylphenidate (MPH). Functional magnetic resonance imaging was used to investigate the effects of a single dose of MPH on brain activation during interference inhibition in medication-nave ADHD boys. Medication-nave boys with ADHD were scanned twice, in a randomized, double-blind design, under either a single clinical dose of MPH or placebo, while performing a Simon task that measures interference inhibition and controls for the oddball effect of low-frequency appearance of incongruent trials. Brain activation was compared within patients under either drug condition. To test for potential normalization effects of MPH, brain activation in ADHD patients under either drug condition was compared with that of healthy age-matched comparison boys. During incongruent trials compared with congruent-oddball trials, boys with ADHD under placebo relative to controls showed reduced brain activation in typical areas of interference inhibition, including right inferior prefrontal cortex, left striatum and thalamus, mid-cingulate/supplementary motor area, and left superior temporal lobe. MPH relative to placebo upregulated brain activation in right inferior prefrontal and premotor cortices. Under the MPH condition, patients relative to controls no longer showed the reduced activation in right inferior prefrontal and striato-thalamic regions. Effect size comparison, furthermore, showed that these normalization effects were significant. MPH significantly normalized the fronto-striatal underfunctioning in ADHD patients relative to controls during interference inhibition, but did not affect medial frontal or temporal dysfunction. MPH therefore appears to have a region-specific upregulation effect on fronto-striatal activation.

……..

Neurosci Lett. 2011;498:190-93.

AUTOMATIC CLASSIFICATION OF HYPERACTIVE CHILDREN: COMPARING MULTIPLE ARTIFICIAL INTELLIGENCE APPROACHES.

Delavarian M, Towhidkhah F, Gharibzadeh S, et al.

Automatic classification of different behavioral disorders with many similarities (e.g. in symptoms) by using an automated approach will help psychiatrists to concentrate on correct disorder and its treatment as soon as possible, to avoid wasting time on diagnosis, and to increase the accuracy of diagnosis. In this study, we tried to differentiate and classify (diagnose) 306 children with many similar symptoms and different behavioral disorders such as ADHD, depression, anxiety, comorbid depression and anxiety and conduct disorder with high accuracy. Classification was based on the symptoms and their severity. With examining 16 different available classifiers, by using " Prtools" , we have proposed nearest mean classifier as the most accurate classifier with 96.92% accuracy in this research.

……..

Pediatrics. 2011;127:e1406-e1413.

CLONIDINE EXTENDED-RELEASE TABLETS AS ADD-ON THERAPY TO PSYCHOSTIMULANTS IN CHILDREN AND ADOLESCENTS WITH ADHD.

Kollins SH, Jain R, Brams M, et al.

OBJECTIVE: To assess the efficacy and safety of clonidine hydrochloride extended-release tablets (CLON-XR) combined with stimulants (ie, methylphenidate or amphetamine) for attention-deficit/hyperactivity disorder (ADHD).

PATIENTS AND METHODS: In this phase 3, double-blind, placebo-controlled trial, children and adolescents with hyperactive- or combined-subtype ADHD who had an inadequate response to their stable stimulant regimen were randomized to receive CLON-XR or placebo in combination with their baseline stimulant medication. Predefined efficacy measures evaluated change from baseline to week 5. Safety was

assessed by spontaneously reported adverse events, vital signs, electrocardiogram recordings, and clinical laboratory values. Improvement from baseline for all efficacy measures was evaluated using analysis of covariance.
RESULTS: Of 198 patients randomized, 102 received CLON-XR plus stimulant and 96 received placebo plus stimulant. At week 5, greater improvement from baseline in ADHD Rating Scale IV (ADHD-RS-IV) total score (95% confidence interval: -7.83 to -1.13; P = .009), ADHD-RS-IV hyperactivity and inattention subscale scores (P = .014 and P = .017, respectively), Conners' Parent Rating Scale scores (P < .062), Clinical Global Impression of Severity (P = .021), Clinical Global Impression of Improvement (P = .006), and Parent Global Assessment (P = .001) was observed in the CLON-XR plus stimulant group versus the placebo plus stimulant group. Adverse events and changes in vital signs in the CLON-XR group were generally mild.
CONCLUSIONS: The results of this study suggest that CLON-XR in combination with stimulants is useful in reducing ADHD in children and adolescents with partial response to stimulants.

……..

Personality and Individual Differences. 2011 Jun;50:1305-08.
THE DIFFERENCE BETWEEN AUTISM AND ADHD IS IN THE EYE OF THE COGNITIVE TASK?
Barnard-Brak L.
A body of literature has indicated shared characteristics of children with autism spectrum disorders (ASDs) and Attention Deficit Hyperactivity Disorder (ADHD). The purpose of the current study was to demonstrate how different cognitive-attentional tasks may distinguish between children with ASDs and ADHD dependent upon the cognitive-attentional task. Multivariate analyses of covariance (MANCOVAs) were performed to determine whether the Leiter-R sustained attention subscale task and a rapid letter naming task distinguished between children with ADHD and ASDs, respectively in Study 1 and Study 2. Leiter-R sustained attention subscale task scores did not distinguish between children with ADHD and ASDs. Rapid letter naming performance, however, did appear to distinguish between children with ADHD and ASDs. Different cognitive-attentional tasks may distinguish differently between children with ADHD and ASDs.

……..

Postgrad Med. 2010;122:27-34.
DOES PRIOR EXPOSURE TO STIMULANTS IN CHILDREN WITH ADHD IMPACT CARDIOVASCULAR PARAMETERS FROM LISDEXAMFETAMINE DIMESYLATE?
Wigal SB, Jun A, Wong AA, et al.
Objective: To evaluate the safety profile, based on cardiovascular measurements, of lisdexamfetamine dimesylate (LDX) in children with and without prior exposure to stimulant medication in the treatment of attention-deficit/hyperactivity disorder (ADHD).
Methods: This single-blind, modified laboratory school study used open-label dose optimization of children aged 6 to 12 years. Lisdexamfetamine dimesylate, initiated at 30 mg, was dose titrated in 20-mg weekly increments to a possible 70 mg over 4 to 5 weeks. Safety outcomes presented in this study were assessed using vital signs (blood pressure and pulse) and electrocardiograms, conducted at baseline and following LDX treatment. Analyses were performed across all subjects, as well as post hoc based on prior treatment status. In addition, hematologic and blood biochemistry analyses were conducted at baseline but not following treatment.
Results: Twenty-eight subjects enrolled in the study, with 27 safety protocol completers (n = 14 prior stimulant exposure; n = 13 stimulant naive). In total, 2 subjects in the stimulant-naive group experienced changes from baseline vital sign measurements outside the normal range: 1 with tachycardia and 1 with blood pressure (greater-than or equal to) 95th percentile of the normal age range. One other subject in the stimulant-naive group experienced prolonged QTc in response to LDX, which resolved at follow-up. Pretreatment laboratory work revealed no differences on any parameters when reviewed by exposure subgroup.

Conclusion: While LDX reduced the core symptoms of ADHD to a similar degree in treatment-naive and previously treated groups of children with ADHD, more cardiovascular effects were measured in stimulant-naive children than in children who had previously been exposed to stimulant treatment. Future controlled studies with larger samples should address the impact of prior stimulant exposure on other ADHD treatments.

……..

Postgrad Med. 2010;122:18-26.

MIGRAINE, TENSION-TYPE HEADACHE, AND ATTENTION-DEFICIT/HYPERACTIVITY DISORDER IN CHILDHOOD: A POPULATION-BASED STUDY.

Arruda MA, Guidetti V, Galli F, et al.

Objectives: Primary headache syndromes (eg, migraine and tension-type headache [TTH]) and attention-deficit/hyperactivity disorder (ADHD) are prevalent in childhood and may cause impairment in social and academic functioning. We tested if ADHD or its symptoms are associated with specific headache syndromes or with headache frequency.

Study design: Cross-sectional epidemiological study with direct interviews to parents and teachers using validated and standardized questionnaires.

Setting: Populational study. Participants: Children aged 5 to 11 years (n = 1856). Outcome measures: Prevalence of ADHD as a function of headache status in crude and adjusted analyses.

Results: The prevalence of migraine was 3.76%. Infrequent episodic TTH occurred in 2.3% of the sample, and frequent episodic TTH occurred in 1.6%. The prevalence of ADHD was 6.1%. The prevalence of ADHD was not significantly different by headache category. For hyperactivity-impulsivity symptoms, the prevalence was 8.1% in children without headache, 23.7% in children with migraine (relative risk [RR], 2.6; 95% confidence interval [CI], 1.6-4.2), and 18.4% in children with probable migraine (RR, 2.1; 95% CI, 1.4-3.2). For inattention, no significant differences were seen. In multivariate analyses, ADHD or inattention symptoms were not predicted by headache subtypes or headache frequency. Hyperactivity-impulsivity symptoms were significantly associated with any headache ($P < 0.01$), TTH ($P < 0.01$), or migraine ($P < 0.001$).

Conclusion: Migraine and TTH are not comorbid to ADHD overall, but are comorbid to hyperactive-impulsive behavior. Providers and educators should be aware of the association.

……..

Postgrad Med. 2010;122:52-61.

DOES PLACEBO RESPONSE DIFFER BETWEEN OBJECTIVE AND SUBJECTIVE MEASURES IN CHILDREN WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER?

Sumner CR, Haynes VS, Teicher MH, et al.

Placebo response complicates the interpretation of treatment response in both clinical practice and clinical trials in youth with attention-deficit/hyperactivity disorder (ADHD). In a pilot study comparing subjective ADHD symptom rating scales with scores obtained using the Quotient(trademark) ADHD System (an objective computerized technology for assessment of hyperactivity, inattention, and impulsivity in ADHD), it was found that agreement between these 2 measures was not as strong as anticipated. This observation prompted us to evaluate placebo responses associated with subjective and objective assessments. Eligible study participants aged 6 to 14 years with a Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition ADHD diagnosis based on clinician interviews were randomized to 1 of 2 treatment sequence groups (placebo, low dose, and medium dose; or low dose, medium dose, and placebo) using either atomoxetine HCl or osmotic controlled-release (OROS) methylphenidate HCl as the active treatment in a 3-week, triple-blind (subject, parent, rater) trial. Subjects were exposed to placebo and different medication doses to evaluate the comparative sensitivity of objective and subjective measures in assessing changes in clinical condition. Placebo response was defined using 3 thresholds: any improvement, > 25% improvement, or > 40% improvement from baseline on Quotient(trademark)Global Scaled Score (QGSS) or

the ADHD Rating Scale (ADHD-RS) Total score from baseline to the visit when placebo was administered. Lin's concordance correlation coefficient was used to measure agreement between baseline and placebo scores for the objective and subjective assessments. Of 30 subjects with placebo and baseline scores, 80%, 47%, and 27% met the 3 response thresholds (ie, any, > 25%, or > 40% improvement, respectively) on the ADHD-RS Total score compared with 27%, 7%, and 0% on the QGSS. Lin's concordance correlation coefficient was 0.81 and 0.39 for the QGSS and the ADHD-RS Total score, respectively. Although larger trials are warranted, we tentatively conclude that using objective measures and higher response thresholds may enhance assay sensitivity in clinical trials and hence limit necessary patient enrollments to rule out type II statistical error.

……..

Postgrad Med. 2010;122:62-68.

THE ASSOCIATION OF BULLYING AND HEALTH COMPLAINTS IN CHILDREN WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.

Holmberg K.

Background: Attention-deficit/hyperactivity disorder (ADHD) in schoolchildren is often associated with troublesome relationships with family members and peers as well as difficulties in the classroom. The aims of this study were to assess the associations between attention-deficit/hyperactivity disorder (ADHD), recurrent subjective health complaints, and bullying in the peer group in schoolchildren.

Method: Cohort study of 577 fourth graders (10-year-olds) in 1 municipality in Stockholm County, Sweden. All children were screened for attention and behavior problems through interviews with their parents and teachers. Children with high scores underwent further clinical and cognitive assessments. Information about health complaints and bullying was collected from the children themselves in a classroom questionnaire. The 516 children for whom there was information from all 3 data sources were included in the final study population.

Results: Attention-deficit/hyperactivity disorder was associated with a 2-fold increased risk for recurrent abdominal pain (RAP), sleeping problems, and tiredness, while there was no association with headache. Bullying other students as well as being bullied were strongly associated with ADHD. There was a 2-fold increased risk for all kinds of health complaints among children being bullied, while bullies were more likely to report tiredness than other children.

Conclusions: Evaluation and treatment strategies for ADHD need to include an effective evaluation and treatment of RAP, tiredness, and sleeping disturbances as well as assessment and effective interventions for bullying. Evaluation of ADHD should be considered in children with recurrent health complaints and in children involved in bullying. Antibullying interventions are important to prevent health problems in all children.

……..

Prev Med. 2011;52:S70-S74.

THE EFFECTS OF PHYSICAL ACTIVITY ON ATTENTION DEFICIT HYPERACTIVITY DISORDER SYMPTOMS: THE EVIDENCE.

Gapin JI, Labban JD, Etnier JL.

Evidence supports the beneficial effects of physical activity (PA) on cognitive performance and suggests that effects might be particularly large for children. However, limited research has explored PA as a means of managing behavioral symptoms and improving cognitive performance of children with attention deficit hyperactivity disorder (ADHD). The etiology of ADHD and the putative mechanisms for the effects of PA on cognitive performance suggest that PA might be especially important for this population. Objective: The purpose of this paper is to review the literature regarding the potential of PA for ADHD symptom management, particularly in regard to behavioral and cognitive symptoms. Methods: Literature was reviewed for published and unpublished research specifically examining the effects of PA on cognitive and/or behavioral symptoms of ADHD. Additionally, potential mechanisms were addressed. Results: Albeit limited, current research generally supports the potential for acute and chronic PA to mitigate ADHD

symptoms. Conclusion: Given the generally supportive extant literature and the challenges that face children with ADHD, future research exploring the potential of PA with this population is advocated.

……..

Progress in Neuro-Psychopharmacology & Biological Psychiatry. 2011 Mar;35:421-28.

ASSOCIATION BETWEEN THE DOPAMINE TRANSPORTER GENE AND THE INATTENTIVE SUBTYPE OF ATTENTION DEFICIT HYPERACTIVITY DISORDER IN TAIWAN.

Shang CY, Gau SS-F, Liu CM, et al.

Attention deficit hyperactivity disorder (ADHD) is a common heritable childhood psychiatric disorder. Since methylphenidate, one of the main drugs used to treat ADHD, targets the dopamine transporter, this study examined the linkage disequilibrium (LD) structure of the dopamine transporter gene (DAT1) and investigated whether the DAT1 gene was associated with ADHD. This Chinese family-based association sample consisted of 273 DSM-IV diagnosed ADHD probands and their family members (n = 906). We screened 15 polymorphisms across the DAT1 gene, including 14 single nucleotide polymorphism (SNP) markers and the variable number of tandem repeat (VNTR) polymorphism in 3'-untranslated region (3'UTR). Calculations of pairwise LD revealed three main haplotype blocks (HBs): HB1 (intron 2 through intron 6), HB2 (intron 8 through intron 11), and HB3 (3'UTR). Family-Based Association Tests showed that no allele was significantly more transmitted than expected to the ADHD children for these 15 markers. Haplotype-Based Association Tests showed that a haplotype rs27048 (C)/rs429699 (T) was significantly associated with the inattentive subtype (P = 0.008). In quantitative analyses, this haplotype also demonstrated significant association with the inattention severity (P = 0.012). Our finding of the haplotype rs27048 (C)/rs429699 (T) as a novel genetic marker in the inattentive ADHD subtype suggests that variation in the DAT1 gene may primarily affect the inattentive subtype of ADHD.

……..

Progress in Neuro-Psychopharmacology & Biological Psychiatry. 2011 Mar;35.

THE POSSIBLE EFFECT OF METHYLPHENIDATE ON SECONDARY ENCOPRESIS IN CHILDREN WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.

Bilgiç A.

Presents the case report of two children with attention deficit hyperactivity disorder (ADHD) and coexisting secondary encopresis who displayed improvement in ADHD symptoms accompanied by complete resolution of encopresis with methylphenidate (MPH) treatment. The first case is an 8 year-old-boy and the second case is a 13-year-old-boy, both diagnosed with ADHD. Their encopretic symptoms have continued for three and seven years without any improvement period. In the first case, MPH slow release treatment was started at 18 mg daily, but only a slight improvement was obtained after a period of 4 weeks. The medication dose was then increased to 27 mg daily. All symptoms decreased markedly in the first week of the 27 mg daily dose and encopretic and enuretic behavior completely stopped in the course of the fifth week of the treatment. In the second case, short acting MPH treatment was commenced at 10 mg twice daily, resulted in moderate improvement in hyperactivity and impulsivity symptoms and complete resolution of the encopresis after the first day of the treatment. But, his attention symptoms did not decrease with MPH treatment. After MPH treatment, these two boys revealed no signs of encopresis over the follow-up period of six and two months, respectively.

……..

Prog Neuro-Psychopharmacol Biol Psychiatry. 2011;35:1349-54.

WORKING MEMORY AND ATTENTION DEFICITS IN ADOLESCENT OFFSPRING OF SCHIZOPHRENIA OR BIPOLAR PATIENTS: COMPARING VULNERABILITY MARKERS .

Diwadkar VA, Goradia D, Hosanagar A, et al.

Background: Working memory deficits abound in schizophrenia and attention deficits have been documented in schizophrenia and bipolar disorder. Adolescent offspring of patients may inherit vulnerabilities in brain circuits that subserve these cognitive domains. Here we assess impairments in offspring of schizophrenia (SCZ-Offspring) or bipolar (BP-Offspring) patients compared to controls (HC) with no family history of mood or psychotic disorders to the second degree.

Methods: Three groups (n = 100 subjects; range: 10-20. yrs) of HC, SCZ-Offspring and BP-Offspring gave informed consent. Working memory was assessed using a delayed spatial memory paradigm with two levels of delay (2. s & 12. s); sustained attention processing was assessed using the Continuous Performance Task-Identical Pairs version.

Results: SCZ-Offspring (but not BP-Offspring) showed impairments in working memory (relative to HC) at the longer memory delay indicating a unique deficit. Both groups showed reduced sensitivity during attention but only BP-Offspring significantly differed from controls.

Conclusions: These results suggest unique (working memory/dorsal frontal cortex) and potentially overlapping (attention/fronto-striatal cortex) vulnerability pathways in adolescent offspring of patients with schizophrenia and bipolar disorder. Working memory and attention assessments in these offspring may assist in the clinical characterization of the adolescents vulnerable to SCZ or BP.

……..

Prog Neuro-Psychopharmacol Biol Psychiatry. 2011;35:939-43.

GRAY MATTER VOLUME DEFICITS ARE ASSOCIATED WITH MOTOR AND ATTENTIONAL IMPAIRMENTS IN ADOLESCENTS WITH SCHIZOPHRENIA.

Kumra S, Ashtari M, Wu J, et al.

Cognitive deficits have been well described in adolescents with schizophrenia, but little is known about the neuroanatomical basis of these abnormalities. The authors examined whether neuropsychological deficits observed in adolescents with schizophrenia were associated with cortical gray matter volume deficits. Volumes of the superior frontal gyrus, anterior cingulate gyrus and orbital frontal lobe were outlined manually from contiguous MR images and automatically segmented into gray and white matter in 52 patients and 48 healthy volunteers. Subjects received a comprehensive neuropsychological test battery, assessing five different functional domains: executive, attention, verbal memory, motor and sensory motor. Children and adolescents with schizophrenia were found to have lower total cortical and lower superior frontal gyrus gray matter volumes and lower test scores across all functional domains compared to healthy volunteers. Among patients, the lower total cortical gray matter volume was associated with worse functioning on the attention and motor domains. Our findings point to widespread, perhaps multifocal, pathology as contributing to cognitive dysfunction in adolescents with schizophrenia.

……..

Psychiatr Pol. 2011;45:367-78.

VISUAL-SPATIAL FUNCTIONS AND ORGANISATION OF GRAPHO-MOTOR ACTIONS IN ADHD CHILDREN.

Borkowska AR, Slopien A, Pytlinska N, et al.

Aim. The aim of the study was to test whether children with a diagnosis of ADHD at the age of 7-16 years have deficits in visual-spatial, visual memory, planning, and organisation of the visual-motor functions.

Methods. The study included 186 unrelated patients aged 7-16 years diagnosed with ADHD. The control group consisted of 156 healthy individuals aged 7-16 years. The methods applied were the Rey-Osterrieth Complex Figure Test (ROCF) and Matching Familiar Figures Test (MFFT).

Results. The number of errors in the MFFT was significantly different between healthy children and children with ADHD combined subtype and a group of inattentive children and combined subtype. There

were no differences between inattentive and healthy children. In the Rey-Osterieth Complex Figure test, statistically significant differences were found between the control group and a group of combined ADHD in the number of points obtained when drawing back and reproduction from memory. In the latter index were also differences between ADHD inattentive children and the combined subtype. Children with ADHD obtained statistically significant different results than healthy children in the drawing category (which were treated as an indicator of the executive functions of planning) but only in reproduction from memory. Quality of the copy does not differentiate the groups.
Conclusions. ROCF and MFFT are useful measures of visual-spatial function and visual memory of children with ADHD. They have less relevance in the assessment of executive functions. Visual-spatial disorders were found only in children with ADHD combined subtype.

……..

Psychiatry Res. 2011 Apr;186:333-37.
BIPOLAR DISORDER CO-MORBIDITY IN CHILDREN WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER.
Donfrancesco R, Miano S, Martines F, et al.
The present study aimed at: (1) exploring rate and clinical features of superimposed bipolar disorder (BD) in Italian children with attention deficit hyperactivity disorder (ADHD), compared with a community sample, matched for age and gender; (2) exploring predictors of BD in ADHD children, by comparing ADHD children with or without superimposed BD. We studied 173 consecutive drug-naïve outpatients with ADHD (156 males and 17 females, mean age of 9.2 ± 2.3 years, age range 6–17.5 years), diagnosed with a clinical interview (Schedule for Affective Disorders and Schizophrenia for School-Age Children-Present and Lifetime Version (K-SADS-PL)); the control group consisted of a community-based sample of 100 healthy children. The rate of children with a diagnosis of BD was higher in the ADHD group (29/173, 16.7%) compared with controls (1/100, 1%), ($P < 0.001$). Among the 29 children with ADHD+BD, 16 (55.2%) had a Bipolar Disorder-Not Otherwise Specified (BD-NOS), and 11 (37.9%) showed ultrarapid cycling. Compared with children with ADHD without BD, they showed a higher rate of combined sub-type (21/29, 72.4%), a higher score at ADHD-Rating Scale (total score and hyperactivity subscale), higher rates of major depression, oppositional defiant disorder and conduct disorder. In summary, children with ADHD present a higher risk for developing a superimposed BD. The identification of clinical features with an increased risk of BD can improve diagnosis, prognosis and treatments.

……..

Psychiatry Res. 2011 Apr;186:338-44.
LACK OF ASSOCIATION BETWEEN RESPONSE OF OROS-METHYLPHENIDATE AND NOREPINEPHRINE TRANSPORTER (SLC6A2) POLYMORPHISM IN KOREAN ADHD.
Lee SH, Kim SW, Lee MG, et al.
This study investigated the relationship between the five common polymorphisms (rs2242446, rs5568, rs5569, rs998424, and rs1616905) in the norepinephrine transporter (NET) gene and the OROS-methylphenidate response in a medication-naïve Korean attention-deficit hyperactivity disorder (ADHD) sample. One hundred thirty-seven patients with ADHD were recruited from the child and adolescent psychiatric outpatient units. The trial was an eight-week, open-label study of OROS-methylphenidate monotherapy, and treatment outcomes were measured using the Korean version of the ADHD Rating Scales-IV (K-ARS) for the parents, the Clinician Global Impression Severity Scale (CGI-S) and the Clinician Global Impression Improvement Scale (CGI-I). Associations between the five NET polymorphisms and the drug response were analyzed using genotype and allele frequencies at each locus. There was no significant difference in genotype and allele distribution for each NET polymorphism between responders and non-responders ($P > 0.05$). There were no significant differences in change of the K-ARS score, change of CGI-S scores or CGI-I scores at 8 weeks among each genotype and allele of five NET

polymorphisms (P > 0.05). Although there were no significant positive results, our findings may have several implications and offer direction for future studies.

……..

Psychol Assess. 2011;23:437-46.
CORRESPONDENCE AND DISPARITY IN THE SELF- AND OTHER RATINGS OF CURRENT AND CHILDHOOD ADHD SYMPTOMS AND IMPAIRMENT IN ADULTS WITH ADHD.
Barkley RA, Knouse LE, Murphy KR.
Experts recommend that clinicians evaluating adults for attention-deficit/hyperactivity disorder (ADHD) obtain information from others who know the patient well. The authors examined correspondence between the self- and other-ratings of ADHD symptoms and impairment using 3 groups of adults recruited on the basis of their severity of ADHD: ADHD diagnosis (n=146), clinical controls self-referring for ADHD but not diagnosed (n=97), and community controls (n=109). The influences of diagnostic group, informant relationship, sex of participant, IQ, and comorbid anxiety and depression on self-informant disparities were also examined. Results indicated moderate to high agreement (59-80) between self and others on current functioning and slightly lower levels (53-75) between self- and parent ratings of childhood functioning. Examination of difference scores between self- and other ratings revealed small mean disparities (-0.1 to +5.0 points) but substantial variation (SDs = -2.4 to 8.9 points) for both current and childhood ratings. Clinic referrals not diagnosed with ADHD, particularly women, had higher disparities than was evident in the ADHD and community groups. Age, IQ, and education were not associated with disparities in most ratings. Higher anxiety, in contrast, was associated with greater disparities on all current and childhood measures of both ADHD and impairment.

……..

Psychological Medicine: A Journal of Research in Psychiatry and the Allied Sciences. 2011 Apr;41:861-71.
THE RELATIONSHIP BETWEEN ADHD AND KEY COGNITIVE PHENOTYPES IS NOT MEDIATED BY SHARED FAMILIAL EFFECTS WITH IQ.
Wood AC, Rijsdijk F, Johnson KA, et al.
Background: Twin and sibling studies have identified specific cognitive phenotypes that may mediate the association between genes and the clinical symptoms of attention deficit hyperactivity disorder (ADHD). ADHD is also associated with lower IQ scores. We aimed to investigate whether the familial association between measures of cognitive performance and the clinical diagnosis of ADHD is mediated through shared familial influences with IQ.
Method: Multivariate familial models were run on data from 1265 individuals aged 6-18 years, comprising 920 participants from ADHD sibling pairs and 345 control participants. Cognitive assessments included a four-choice reaction time (RT) task, a go/no-go task, a choice-delay task and an IQ assessment. The analyses focused on the cognitive variables of mean RT (MRT), RT variability (RTV), commission errors (CE), omission errors (OE) and choice impulsivity (CI).
Results: Significant 'familial association (rF) was confirmed between cognitive performance and both ADHD (rF = 0.41-0.71) and IQ (rF= -0.25 to -0.49). The association between ADHD and cognitive performance was largely independent (80-87%) of any contribution from etiological factors shared with IQ. The exception was for CI, where 49 % of the overlap could be accounted for by the familial variance underlying IQ.
Conclusions: The aetiological factors underlying lower IQ in ADHD seem to be distinct from those between ADHD and RT/error measures. This suggests that lower IQ does not account for the key cognitive impairments observed in ADHD. The results have implications for molecular genetic studies designed to identify genes involved in ADHD.

……..

Psychology of Addictive Behaviors. 2011 Jun;25:320-29.

CHILDHOOD ADHD SYMPTOMS AND RISK FOR CIGARETTE SMOKING DURING ADOLESCENCE: SCHOOL ADJUSTMENT AS A POTENTIAL MEDIATOR.

Flory K, Malone PS, Lamis DA.

Although a large body of research suggests that children with attention-deficit/hyperactivity disorder (ADHD) are at increased risk for cigarette smoking during adolescence compared with their non-ADHD peers, much less research has examined why. The current study addressed this gap in the literature by examining middle school adjustment, broadly defined, as a possible mediator of the relation between childhood ADHD symptoms and cigarette smoking during middle adolescence (10th grade). Longitudinal data were collected from a community sample of 754 youth using self-report and parent report along with school records, and a novel statistical technique was used in the process of testing for mediation. Consistent with hypotheses, school adjustment was found to mediate the relation between childhood ADHD symptoms and later cigarette smoking, even after controlling for early externalizing problems. Results have implications for etiological theories of adolescent deviant behavior and suggest that successful smoking prevention programs targeting youth with ADHD should include a school adjustment component.

……..

Redox Rep. 2011;16:45-46.

EVALUATION OF OXIDATIVE STRESS STATUS IN CHILDREN WITH PERVASIVE DEVELOPMENTAL DISORDER AND ATTENTION DEFICIT HYPERACTIVITY DISORDER USING URINARY-SPECIFIC BIOMARKERS.

Kawatani M, Tsukahara H, Mayumi M.

Pervasive developmental disorder (PDD) and attention deficit hyperactivity disorder (ADHD) are likely to be associated with increased oxidative stress, particularly that of lipid peroxidation. We evaluated the oxidative stress status of pediatric PDD and ADHD patients using their urine samples. Urinary acrolein-lysine levels in 11 PDD and 10 ADHD children (205 (plus or minus) 97 and 234 (plus or minus) 75 nmol/mg Cr, respectively) appeared higher than those of the control subjects (155 (plus or minus) 59 nmol/mg Cr). Measurement of urinary specific biomarkers is comfortable, non-invasive, and easy to perform in children. Our findings might provide a scientific guide for use in further clinical and biochemical studies of these disorders.

……..

Res Dev Disabil. 2011;32:1631-37.

ASSISTING CHILDREN WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER ACTIVELY REDUCES LIMB HYPERACTIVE BEHAVIOR WITH A NINTENDO WII REMOTE CONTROLLER THROUGH CONTROLLING ENVIRONMENTAL STIMULATION.

Shih CH, Yeh JC, Shih CT, et al.

The latest studies have adopted software technology which turns the Wii Remote Controller into a high-performance limb action detector, we assessed whether two persons with multiple disabilities would be able to control an environmental stimulus through limb action. This study extends the functionality of the Wii Remote Controller to the correction of limb hyperactive behavior to assess whether two children with Attention Deficit Hyperactivity Disorder (ADHD) would be able to actively reduce their limb hyperactive behavior through controlling their favorite stimuli by turning them on/off using a Wii Remote Controller. An ABAB design, in which A represented the baseline and B represented intervention phases, was adopted in this study. Result showed that both participants significantly increased their time duration of maintaining a static limb posture (TDMSLP) to activate the control system in order to produce environmental stimulation in the intervention phases. Practical and developmental implications of the findings are discussed.

……..

Res Dev Disabil. 2011;32:1343-50.

EVALUATING PHYSICAL ACTIVITY USING ACCELEROMETRY IN CHILDREN AT RISK OF DEVELOPMENTAL COORDINATION DISORDER IN THE PRESENCE OF ATTENTION DEFICIT HYPERACTIVITY DISORDER.

Baerg S, Cairney J, Hay J, et al.

Physical activity (PA) is compromised in children and adolescents with developmental coordination disorder (DCD). Approximately half of all children with DCD suffer from attention-deficit hyperactive disorder (ADHD); a cohort often considered more physically active than typically developing youth. Accelerometry is an effective method of assessing physical activity patterns; although estimates of PA in children with DCD using this quantifiable method have not been attempted. We hypothesize that children with co-morbid DCD/ADHD will be more physically active than children with DCD and healthy peers. Therefore, the purpose of this study was to contrast physical activity (step count and activity energy expenditure using accelerometry [AEE]) between children with DCD, co-morbid DCD and ADHD (DCD/ADHD), and healthy controls. A sample of 110 children with DCD (N= 32), DCD/ADHD (N= 30) and controls (N= 48) age 12-13. years agreed to participate. Co-morbid DCD/ADHD was present in nearly half of the children with DCD (48.4%). Analysis of covariance demonstrated a positive interaction for females step count ($F[1,92] = 4.92$, $p= 0.009$). A significant group difference for step count ($F[1,92] = 4.43$, $p= .04$) was identified in females. Post hoc comparison tests identified significantly lower step count between males with DCD and controls ($p= .004$) and males with DCD/ADHD and controls ($p= 0.003$). Conversely, females with DCD/ADHD had significantly more step counts than their controls ($p= .01$). Hyperactivity in females with DCD/ADHD appears to contribute to more physical activity, whereas DCD may contribute to decreased activity in males with DCD and DCD/ADHD. Hyperactivity expressed among girls with DCD/ADHD appears to override the hypoactive behavior associated with females with DCD. Conversely, the expression of hyperactivity among boys with DCD/ADHD does not translate as hypothesized. The contrasting expression of physical activity (i.e., step count and AEE) evaluated using accelerometry in boys and girls with DCD, co-morbid DCD/ADHD and healthy peers are intriguing and constitute further investigation in a larger investigation.

……..

Res Dev Disabil. 2011;32:1260-69.

COMORBID ADHD AND DCD: EXAMINING COGNITIVE FUNCTIONS USING THE WISC-IV.

Loh PR, Piek JP, Barrett NC.

This study explored the cognitive performance of children with Attention Deficit/Hyperactivity Disorder (ADHD) and/or Developmental Coordination Disorder (DCD) using the Wechsler Intelligence Scale for Children-IV. Participants were 62 children with ages between 9 years 8 months and 12 years 7 months. These children were placed into one of the four groups: Comparison (n= 26), ADHD (n= 14), DCD (n= 11), and ADHD+. DCD (n= 11) groups. The ADHD symptoms were assessed using the Australian Disruptive Behaviours Scale, and motor ability was assessed using the McCarron Assessment of Neuromuscular Development (MAND). Significantly poorer perceptual reasoning ability was seen in DCD and ADHD+. DCD groups but not in the ADHD group. The findings provide evidence that a deficit in visuo-spatial ability may underlie DCD but not ADHD. These findings revealed different cognitive profiles for ADHD and/or DCD, thus the current study does not lend support to the common aetiology hypothesis in understanding the basis of ADHD and DCD comorbidity.

……..

Rev Neurol. 2011;52:527-35.

QUANTIFICATION AND CONCORDANCE ASSESSMENT AMONG PARENTS AND TEACHERS IN ATTENTION DEFICIT HYPERACTIVITY DISORDER DIAGNOSIS.

Caceres J, Herrero D.

Introduction. Attention deficit hyperactivity disorder (ADHD) is the disorder with higher referral rate to child mental health community centres. Diagnostic criteria are well defined and known by trained clinicians, but they cannot observe children daily and through different settings, and must rely on information offered by

multiple informants (parents, teachers…). To be considered a disorder, it must occur in more than one setting. This extra information is frequently obtained through validated questionnaires.
Aims. To compare percentage of children considered ADHD by their context and those who do meet the criteria, after proper assessment; to assess if there are differences in ratings made by parents and teachers, and to contrast them with deficit obtained through objective tests.
Subjects and methods. 127 children referred to a Mental Health Community Centre were assessed through clinical interview, semi structured observation of family dynamics in one-way mirror room, Conners' questionnaire, filled out by parents and teachers, and WISC subscales.
Results. Only 46% met the criteria to be considered ADHD. Agreement between parents and teachers was low. Parents rated in similar ways boys and girls, but teachers considered boys more inatent and impulsive/hyperactive than girls.
Conclusions. Not only clearly spelled out diagnostic criteria are needed, but steps to reach diagnosis. Proposals are presented to potentiate the assessment process that permits to individualize treatment.

……..

The American Journal of Psychiatry. 2011 Mar;168:329-30.

SELF-REPORTED INCIDENCES OF MOVING VEHICLE COLLISIONS AND CITATIONS AMONG DRIVERS WITH ADHD: A CROSS-SECTIONAL SURVEY ACROSS THE LIFESPAN.

Cox DJ, Cox BS, Cox JC.

This aim of this study is to describe that the collision and citation rates decline with maturation for middle-age drivers with ADHD as with the general population. “ADHD and Driving Safety” survey was placed on five ADHD-related web sites inquiring about the type of ADHD and frequency of citations and collisions in the previous 12 months. Over 6 months, 156 male and 283 female licensed drivers with ADHD completed the survey. The sample was divided into three age groups: adolescents (16–18 years old, N=142), young adults (19–24 years old, N=161), and middle-aged adults (25–62 years old, N=136). Although most (60%) middle-aged male drivers reported no collisions, these findings suggest that vehicular collisions and citations do not decrease with maturation for male drivers with ADHD. Additional research is needed for replication and to explore causal factors. This study design was limited by its cross-sectional, self-report, and nonrandomized nature. For example, there may be a cross-sectional cohort effect, where older men might be more reckless drivers in general and less likely to use ADHD medication. However, this sample is unique in its size, age range, number of women, and geographic scope.

……..

Turk Klin Pediatr. 2011;20:131-37.

IS THE USE OF ROUTINE EEG NECESSARY IN ATTENTION DEFICIT HYPERACTIVITY DISORDER?

Yildirim V, Komur M, Toros F, et al.

Objective: Attention deficit hyperactivity disorder (ADHD) is a common case in all children psychiatry departments. In this study, our objective is to investigate the electroencephalography (EEG) abnormalities in children with ADHD for the following issues: the frequency of EEG abnormalities and their types, whether unnecessary EEG requests are placed for ADHD cases, the relationships between ADHD subtypes and EEG abnormalities, and the relationships between ADHD comorbitiditives and EEG abnormalities.
Material and Methods: This study is conducted by examining the files of 374 previous ADHD cases according to the diagnosis criteria of DSM-IV at the children psychiatry department of the Faculty of Medicine in Mersin University, between the dates of July 2006-September 2007. 49 cases that had incomplete data or repetitive records have been excluded from the study. The remaining 325 cases have been statistically-investigated.
Results: The patients involved in the study were 54 (16.6%) females and 271 (83.4%) males. The average of ages patients were 11.10 (plus or minus) 2.68 years. The reasons of admissions were classified as: 29.2% behavioural disorders, 20.6% hyperactivity, 50.2% school problems. 4.9% of the cases had physical and the 2.2% had some neurological abnormalities 8% came with the stories of paroxysm and 4.9% got the

diagnosis of epilepsy. Upon the analysis of EEG records it was found out that 6.8% of the cases had baseline disorders or slowness, 11.4% had epileptiform abnormalities. 28% of the epileptiform abnormalities were generalized and 72% of those were partial ones.
Conclusion: In our study, similar to other studies in literature it is observed that ADHD cases without neurological treatment abnormalities had 8.9% epileptiform abnormalities. Absence epilepsy and the related EEG abnormalities that should be excluded while ADHD distinctive diagnoses were being performed, were not observed in any cases of our study. As a result, we believe that before an EEG request, a careful neurological treatment, and a detailed story of paroxysm and epilepsy will reduce the number of EEG requests.

……..

Zeitschrift für Neuropsychologie. 2011 Mar;22:7-20.
DIE ENTWICKLUNG INTELLEKTUELLER FÄHIGKEITEN BEI KINDERN MIT ADHS IM LANGZEITVERLAUF — ERGEBNISSE DER 8,5-JAHRE-KATAMNESE DER KÖLNER ADAPTIVEN MULTIMODALEN THERAPIESTUDIE (KAMT).
Schürmann S, Breuer D, Metternich-Kaizman TW, et al.
The intelligence level and profile of adolescents aged 16–22 years, who have received a multimodal treatment of their Attention-Deficit-Hyperactivity-Disorder in their childhood was assessed in a 8.5 year follow-up-study with the K-TIM. The effects of age, gender and type of school were analyzed. The Composite Intelligence-Scale (IQ 91),Crystallized and Fluid Scales were in the lower average range. The fluid was higher than the crystallized intelligence. Current performance was compared with the performance at beginning (IQ 96) and end (IQ 102) of intensive treatment using the K-ABC. The longitudinal analyses show correlations in the medium range. In multiple regression analyses the achievement scale at the end of the treatment had the highest influence on the K-TIM total score with nearly 50% of variance explained.

SHORT COMMUNICATION

CNS Drugs 2011; 25 (6): 503-509
1172-7047/11/0006-0503/$49.95/0

Lower IQ is Associated with Decreased Clinical Response to Atomoxetine in Children and Adolescents with Attention-Deficit Hyperactivity Disorder

Luigi Mazzone,[1] *Laura Reale*,[1] *Valeria Mannino*,[1] *Mariadonatella Cocuzza*[1] and *Benedetto Vitiello*[2]

1 Division of Child Neurology and Psychiatry, Department of Pediatrics, University of Catania, Catania, Italy
2 Child and Adolescent Treatment and Preventive Intervention Research Branch, National Institute of Mental Health, Bethesda, Maryland, USA

Abstract

Objectives: Atomoxetine is commonly used to treat attention-deficit hyperactivity disorder (ADHD) in children with a broad range of cognitive abilities. We examined the association between level of cognitive functioning as determined by IQ and clinical response during treatment with atomoxetine.

Methods: The records of all the children and adolescents treated with atomoxetine at a university clinic in Catania, Italy, over a 3-year period were examined. A total of 55 clinically referred children and adolescents (aged 5–15 years, 53 males) with ADHD were treated with atomoxetine (10–110 mg/day; mean: 1.28 mg/kg/day) for a period ranging from 2 to 168 weeks (mean: 57.3 ± SD 39.4, median: 56). The IQ was assessed as part of the diagnostic evaluation prior to starting treatment. During treatment, clinical outcome was rated on the Clinical Global Impression-Improvement (CGI-I) and CGI-Severity (CGI-S) scales.

Results: The IQ ranged from 43 to 117 (mean: 80.6 ± SD 18.6, median: 84). The IQ and final CGI-I scores were negatively correlated ($r = -0.68$; $p < 0.01$). Children and adolescents with an IQ <85 were less likely to be responders (defined as a final CGI-I score of 1 or 2) than children and adolescents with an IQ ≥85 (20.71% vs 76.9%; $p < 0.001$). None of the patients discontinued atomoxetine due to adverse effects, while treatment was discontinued in 20 subjects due to a lack of efficacy or ambivalence of parents about pharmacological treatment.

Conclusions: Atomoxetine appears to be less effective in children and adolescents with an IQ <85 than in children and adolescents in the average range of cognitive functioning. This difference is not accounted for by differences in the severity of ADHD symptoms, co-morbidity or reduced tolerability to the

medication. These findings suggest that, in order to be fully informative, clinical trials of medications for ADHD should also include children and adolescents functioning in the borderline and cognitive disability range.

Introduction

The efficacy of atomoxetine in the treatment of attention-deficit hyperactivity disorder (ADHD) is supported by a number of controlled trials conducted in children with normal cognitive capacity.[1,2] These studies indicate that atomoxetine, even though less effective than methylphenidate, decreases the symptoms of ADHD with a medium effect size compared with placebo. In clinical practice, atomoxetine is also commonly used to treat children and adolescents with an IQ in the range of intellectual disability (≤70) or at the lower range of normality (between 71 and 84). Although there are indications that methylphenidate is less effective for children with developmental delays and associated cognitive impairment and that IQ moderates response to stimulant medication in children of normal intellect,[3] it is unknown if IQ acts as a moderator of treatment effect also for atomoxetine.

A recently reported search for predictors of atomoxetine efficacy did not identify any demographics or clinical variables associated with treatment outcome.[4] However, while these analyses included variables such as co-morbidity and type of ADHD, they did not account for the level of cognitive functioning as a possible predictor of response. In an open-label study in children with an IQ <62, atomoxetine was associated with significant improvement over baseline, with a symptomatic improvement in 88% of the patients, a positive response in 62% and remission or clinical normalization in 20%. However, because of the lack of a control, possible treatment effects cannot be distinguished from time effects.[5] A few studies of atomoxetine in children with pervasive developmental disorders, with response rates ranging from 60% to 75%, have been reported, but two involved only participants with an IQ of at least 70,[6,7] and another, although placebo controlled, had a small sample size and did not report on possible effects of IQ on treatment response.[8]

We examined the records of all the children and adolescents treated with atomoxetine at the University of Catania Medical School Department of Child and Adolescent Neuropsychiatry, Catania, Italy, during a 3-year period. In Italy, stimulant medications are seldom used in the treatment of ADHD, which is primarily managed with behavioural interventions. If pharmacotherapy is warranted, parents often opt for atomoxetine. Based on the data on stimulants, we hypothesized that lower cognitive functioning as determined by a lower IQ would be associated with lower efficacy of the medication.

Method

Sample Identification

A systematic review of the medical records of all the children and adolescents treated with atomoxetine at the Child and Adolescent Department of Neuropsychiatry of the University of Catania, Catania, Italy, between January 2007 and July 2010 was conducted. The following information was extracted: demographics, IQ (routinely assessed in all patients as part of their intake evaluation), psychiatric diagnoses by the administration of the Kiddie-Schedule for Affective Disorders and Schizophrenia-Present and Lifetime Version (K-SADS-PL)[9] interview to the parents, history of previous treatment, Parent Swanson, Nolan, and Pelham Rating Scale-IV (SNAP-IV) at baseline, clinician-rated Clinical Global Impression-Improvement (CGI-I) at endpoint and CGI-Severity (CGI-S) scales[10] at baseline and through endpoint.

The ADHD diagnosis was made according to the DSM IV-TR criteria, while the K-SADS-PL was used to collect the clinical information. In addition, at least six of the inattention and/or hyperactivity/impulsivity items of the SNAP-IV

had to be scored "pretty much" or higher for diagnosis accuracy.

The IQ was measured with the Wechsler Intelligence Scale for Children-III edition (WISC-III),[11] and yielded, in addition to a full-scale total score (IQ), a verbal (VIQ) and a performance (PIQ) score. The WISC-III was used because the WISC-IV was not available in Italian.

Assessments

The SNAP-IV[12] is a revision of the Swanson, Nolan and Pelham (SNAP) Questionnaire. The items from the DSM-IV criteria for ADHD are included in the SNAP-IV for the two subsets of symptoms: inattention (item numbers 1–9) and hyperactivity/impulsivity (item numbers 10–18). Also, items are included from the DSM-IV criteria for oppositional defiant disorder (ODD) [item numbers 19–26] since this disorder is often present in children and adolescents with ADHD. The SNAP-IV was used to characterize the severity of illness at baseline, but not for measuring treatment response.

Severity of illness and improvement during treatment were rated by the treating clinicians on the CGI-S and CGI-I scales. The CGI-S scale is a 7-point scale that requires the clinician to rate the current severity of the patient's illness (1 = normal, not at all ill; 2 = borderline mentally ill; 3 = mildly ill; 4 = moderately ill; 5 = markedly ill; 6 = severely ill; or 7 = extremely ill). Likewise, the CGI-I scale requires the clinician to assess how much the patient's illness has improved or worsened relative to a baseline state on a 7-point scale (1 = very much improved; 2 = much improved; 3 = minimally improved; 4 = no change; 5 = minimally worse; 6 = much worse; or 7 = very much worse). Clinical response was defined as a final CGI-I score of 1 or 2. The raters were child neuropsychiatrists at the university clinic, who had been trained in the reliable use of these scales, as shown by scoring at least three tapes of clinical cases according to the gold standard.

Data Analysis

Standard descriptive statistics, chi-square or Fisher's exact tests, Pearson's r correlations and linear regression models were applied to the data in order to evaluate the association between the clinical and cognitive variables at baseline and during treatment. The association between cognitive level and clinical improvement was further explored after categorizing the sample based on an IQ below versus equal to or above one or two SDs below the normative mean (i.e. 85 and 70, respectively).

An α level of 0.05 was set for statistical significance. All the analyses were performed using the Statistical Package for Social Sciences (SPSS® 14.0 for Windows; distributed by IBM, Armonk, NY, USA).

Results

Baseline Pre-Treatment Characteristics

A total of 55 patients aged 5–15 years (53 males, 2 females; IQ range: 43–117, mean: 80.6 ± SD 18.6, median: 84) with a DSM-IV[13] diagnosis of ADHD (96% with combined subtype and 4% with hyperactive subtype) were treated with atomoxetine (table I). Twenty-six children and adolescents had an IQ ≥85 (range: 85–117, mean: 95.9 ± 9.2) and 29 children and adolescents had an IQ <85 (range: 43–84, mean: 66.9 ± 13.3). Seventeen of the children and adolescents in the IQ <85 subgroup met criteria for intellectual disability; these children and adolescents had an IQ ≤70 (range: 42–70, mean: 57.9 ± 9.7), with a significant impairment clinically evaluated in adaptive behaviour in at least two domains. They did not differ from the rest of the sample with respect to age ($p = 0.31$), sex distribution ($p = 0.53$), SNAP-IV ($p = 0.64$) or CGI-S ($p = 0.26$) scores, or co-morbidity with ODD ($p = 1.0$). Moreover, 27 of all subjects (49%) also met criteria for ODD, with no difference in the rate of co-morbid ODD between the IQ subgroups (13 patients with ODD in the subgroup with an IQ ≥85 and 14 in those with an IQ <85).

No child met criteria for ADHD inattentive type, and the severity of inattentive symptoms, as measured on the SNAP-IV Inattentive Subscale, was similar across the IQ subgroups.

The patients had not received prior treatment with atomoxetine, stimulants or other psychotropic medications. All patients received behavioural

Table I. Baseline demographics and clinical characteristics

	All	IQ <85	IQ ≥85	p-Value[a]
N	55	29	26	
Sex (male : female)	53 : 2	28 : 1	25 : 1	1.00
Age [y, mean (SD)]	9.9 (2.4)	10.0 (2.8)	9.8 (1.9)	1.00
range	5–15	5–15	6–13	
IQ [mean (SD)]	80.6 (18.6)	66.9 (13.3)	95.9 (9.2)	
range	43–117	43–84	85–117	
VIQ [mean (SD)]	84.7 (17.5)	72.4 (12.2)	97.4 (12.5)	
range	51–128	51–91	76–128	
PIQ [mean (SD)]	81.7 (18.1)	68.6 (14.5)	95.2 (9.5)	
range	45–123	45–106	82–123	
ADHD subtype [n (%)]				1.00
inattentive	0 (0)	0 (0)	0 (0)	
hyperactive/impulsive	2 (3.6)	1 (3.4)	1 (3.8)	
combined	53 (96.36)	28 (96.55)	25 (96.15)	
SNAP-IV [mean (SD)]	41.1 (5.8)	41.2 (6.0)	41.0 (5.7)	0.91
range	29–51	30–51	29–50	
CGI-S [mean (SD)]	5.5 (0.9)	5.6 (0.9)	5.38 (0.8)	0.31
range	4–7	4–7	4–7	

a Student's t-test for continuous variables and Fisher's exact test for categorical variables.

ADHD = attention-deficit hyperactivity disorder; **CGI-S** = Clinical Global Impression-Severity Scale; **PIQ** = performance score; **SNAP** = Parent Swanson, Nolan, and Pelham Rating Scale; **VIQ** = verbal score.

interventions for the management of ADHD in addition to atomoxetine. None of these patients met criteria for an autism spectrum disorder, mood disorder or anxiety disorder according to DSM-IV-TR criteria or had a history of seizures.

No correlation between the IQ and SNAP-IV ($r = -0.04$; $p = 0.77$) or CGI-S ($r = -0.14$; $p = 0.31$) was detected. Age was not correlated with the IQ ($r = 0.04$; $p = 0.78$), CGI-S ($r = -0.03$; $p = 0.82$), SNAP-IV Inattentive Subscale ($r = 0.07$; $p = 0.62$) or SNAP-IV Hyperactivity/Impulsivity Subscale ($r = -0.25$; $p = 0.07$) scores. The subgroup with an IQ <85 ($n = 29$) was aged 5–15 years (mean: 10.03 ± 2.76 years), and the subgroup with an IQ ≥85 ($n = 26$) was aged 6–13 years (mean: 9.77 ± 1.94 years); these subgroups did not differ significantly in age, gender or SNAP-IV scores (table I).

Atomoxetine Treatment

Atomoxetine was started at a dosage of 0.5 mg/kg/day and gradually increased based on clinical response. The mean duration of treatment was 57.3 weeks (SD 39.45, range: 2–168, median: 56 weeks), and did not differ between the IQ ≥85 and IQ <85 subgroups. The mean final dosage was 1.28 mg/kg/day (SD 0.39, range: 0.32–1.76). The final dosage did not differ in the subgroup with an IQ <85 (1.29 ± 0.49 mg/kg/day) as compared with the subgroup with an IQ ≥85 (1.27 ± 0.31 mg/kg/day; $p = 0.86$). In the IQ <70 subgroup the duration of treatment (43.76 ± 27.98 weeks; $p = 0.07$) and the final dosage (1.21 ± 0.59 mg/kg/day; $p = 0.59$) also did not differ from those in the IQ >70 subgroup (64.21 ± 41.64 weeks; 1.30 ± 0.30 mg/kg/day).

The most common adverse effects were as follows: loss of appetite ($n = 13$), abdominal pain ($n = 12$), nausea ($n = 7$), weight loss ($n = 4$), vomiting ($n = 3$), sleepiness ($n = 2$), paraesthesia ($n = 1$) and mydriasis ($n = 1$). These adverse effects were transient, and no patient discontinued treatment because of adverse effects. The rate or severity of adverse effects did not differ between the IQ subgroups.

The parents of 20 patients decided to discontinue treatment after relatively short periods of time, usually for lack of sufficient improvement and, in some cases, ambivalence about pursuing pharmacological treatment for their child.

IQ and Clinical Improvement

The end of treatment CGI-I score was negatively correlated with the IQ (n = 55, r = –0.679; p < 0.01) [figure 1], as well as the VIQ (r = –0.61; p < 0.01) and the PIQ (r = –0.69; p < 0.01). In the subgroup with an IQ <85 (n = 29), the IQ was negatively correlated with final CGI-I (r = –0.46; p = 0.01) and CGI-S (r = –0.45; p = 0.02) scores. However, in the group with an IQ ≥85 (n = 26), there was no correlation between the IQ and CGI-I (r = –0.036; p = 0.86) or CGI-S (r = 0.105; p = 0.61) scores.

Severity of illness scores showed a greater decline during treatment with atomoxetine in the IQ ≥85 subgroup than in the IQ <85 subgroup (figure 2). Response, defined as a final CGI-I score of 1 or 2, was more likely in children and adolescents with an IQ ≥85 (20 of 26, 76.9%) than in those with an IQ <85 (6 of 29, 20.7%, Fisher's exact test: p < 0.001). The response rate was even smaller in the subgroup functioning in the intellectual disability range (i.e. with an IQ ≤70), with only 1 child of 17 being a responder, a rate that was significantly lower than that observed among children and adolescents with an IQ >70 (25 of 38, 65.8%, $X^2 = 14.59$; p < 0.01; figure 3). Analyses of the response rates using the VIQ or the PIQ yielded similar results to those based on the full scale IQ.

Discussion

This is the first study, to our knowledge, that has examined the relationship between IQ and atomoxetine effectiveness. After systematically reviewing consecutively treated children and adolescents with ADHD, we found that atomoxetine was significantly less effective in patients with lower cognitive functioning (figures 1 and 2). Among children and adolescents with an IQ ≤70, only 6% showed significant improvement (figure 3). The negative impact of IQ on treatment response was not evident in children and adolescents functioning in the average or above average range of intelligence. The effect of IQ on treatment response could not be explained by differences in the severity of ADHD, which was not related to the IQ at baseline.

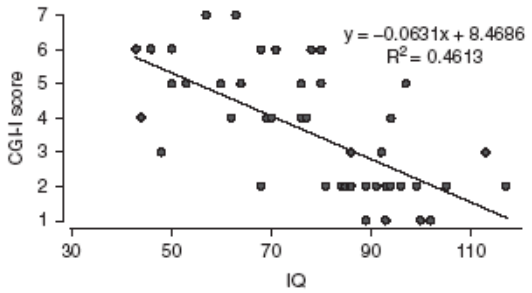


Fig. 1. IQ and improvement during atomoxetine treatment. **CGI-I** = Clinical Global Impression-Improvement Scale.

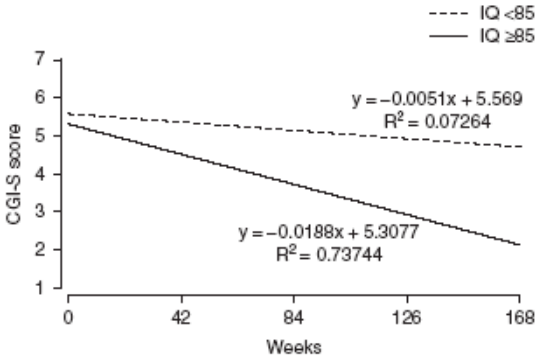


Fig. 2. Severity of illness estimated scores during atomoxetine treatment by IQ subgroup. **CGI-S** = Clinical Global Impression-Severity Scale.

It is possible that the methods used to ascertain ADHD symptoms may be less sensitive to detect treatment effects in children and adolescents with a lower IQ. Recognizing a clinical response in subjects with a lower IQ can be more challenging than in patients with a higher IQ. An improvement in attention and concentration may be masked by the functional impairment caused by the intellectual disability.

Our findings are consistent with reports that methylphenidate, a stimulant commonly used to treat ADHD, is less effective in children and adolescents with intellectual disabilities or pervasive developmental disorders.[14,15] While one study reported that children with an IQ ranging from 50 to 74 responded to methylphenidate at a rate consistent with that observed in children with normal cognitive functioning,[16] within the range of cognitive disability (i.e. an IQ <70), a lower IQ was found to predict poorer response to

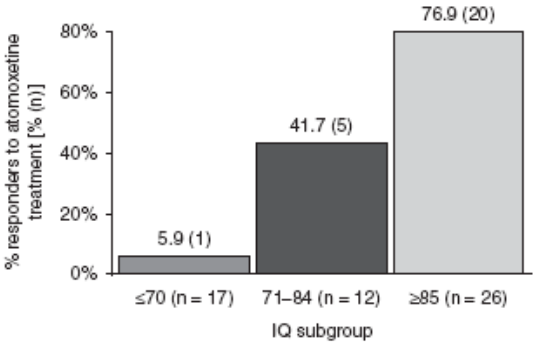


Fig. 3. Rate of response by IQ subgroup. Response: final Clinical Global Impression-Improvement Scale (CGI-I) score of 1 (very much improved) or 2 (much improved). This figure shows data from the full scale IQ; similar results were obtained using a verbal IQ or a performance IQ.

methylphenidate, as children with a moderate to severe degree of intellectual disability showed less improvement in ADHD symptoms than children with mild to borderline intellectual disability.[17] The IQ was also found to be a moderator of response to treatment with methylphenidate in children with ADHD and an IQ of ≥80, in the direction of a better response with a higher IQ.[3] These data suggest that pharmacological treatment of ADHD is in general less effective in children with a lower IQ, and that this finding is not specific to atomoxetine. In our sample, however, the IQ did not influence the tolerability to atomoxetine, while methylphenidate has been reported to be more likely to induce intolerable adverse effects in children with autism and a low IQ (18%) than in children with ADHD who are otherwise normally developing.[15]

There may be specific biological differences underlying differences in efficacy by IQ. Atomoxetine acts through selectively increasing dopamine transmission at the prefrontal cortex level,[18] and several studies have shown a dysfunction in the dopaminergic and adrenergic transmission in the prefrontal cortex of individuals with idiopathic intellectual disabilities.[19] It is possible that these abnormalities impair the efficacy of pharmacological treatment.

The present study has a number of limitations that must be taken into account in interpreting the data. First, this was a retrospective analysis of naturalistically treated children and adolescents. Even though these patients were consecutively treated at a specialized neuropsychiatric clinic, the uncontrolled nature of the study prevents conducting moderator analyses. Second, the sample size was relatively small. Third, the patients were derived from a homogeneous ethnic background and geographical context, all coming from a single university clinic, and may not represent other clinical settings. Finally, although parents provided detailed information on school performance and behaviour, teacher SNAP-IV scores were not consistently obtained to assess drug response accurately. Despite these important limitations, a clear-cut inverse relationship between IQ and degree of improvement was evident.

These findings may have important implications for both clinical practice and further research. Atomoxetine is often used for the treatment of children and adolescents with ADHD in the context of a low IQ. Clinicians should be alert to the possibility that the medication may be less likely to be effective in these patients. As this situation does not seem to be specific to atomoxetine, but also to stimulant medications, there may be structural differences between ADHD in individuals with low cognitive functioning versus those with ADHD and a higher IQ. While psychometrically valid rating scales, such as the Aberrant Behavior Checklist,[20] are available for children with intellectual impairment, and novel approaches focused on individually targeted symptoms have been introduced,[21] research to develop more sensitive and specific assessment instruments for evaluating ADHD symptoms in children and adolescents with a lower IQ may be warranted. Regulatory clinical trials for ADHD medications typically exclude children with a lower IQ. However, extrapolating data from these trials to children with a lower IQ may overestimate the effectiveness of medications in these patients.

Conclusions

A lower IQ among children and adolescents with ADHD was found to be strongly associated with decreased benefit from atomoxetine treatment. If replicated, these findings suggest that, in

order to be fully informative for clinical practice, future trials of medications for ADHD should study subjects with a broad range of cognitive abilities, including also children and adolescents with a lower IQ and cognitive disabilities.

Acknowledgements

Luigi Mazzone and Laura Reale contributed equally to this work in terms of realization of the study, data analysis and paper writing. Valeria Mannino and Mariadonatella Cocuzza collected the data, and Benedetto Vitiello contributed to the design of the study, supervised statistical analysis and helped in the theoretical interpretation of the results. This study was funded by the Division of Child Neurology and Psychiatry of the University of Catania, Catania, Italy. Dr Mannino received educational travel funds by Eli Lilly. The other authors (LM, LR, BV) have no relevant financial disclosures.

References

1. Michelson D, Faries D, Wernicke J, et al., Atomoxetine ADHD Study Group. Atomoxetine in the treatment of children and adolescents with attention-deficit/hyperactivity disorder: a randomized, placebo-controlled, dose-response study. Pediatrics 2001; 108 (5): E83
2. Newcorn JH, Kratochvil CJ, Allen AJ, et al., Atomoxetine/Methylphenidate Comparative Study Group. Atomoxetine and osmotically released methylphenidate for the treatment of attention deficit hyperactivity disorder: acute comparison and differential response. Am J Psychiatry 2008 Jun; 165 (6): 721-30
3. Owens EB, Hinshaw SP, Kraemer HC, et al. Which treatment for whom for ADHD? Moderators of treatment response in the MTA. J Consult Clin Psychology 2003; 71 (3): 540-52
4. Scott NG, Ripperger-Suhler J, Rajab MH, et al. Factors associated with atomoxetine efficacy for treatment of attention-deficit/hyperactivity disorder in children and adolescents. J Child Adolesc Psychopharmacol 2010; 20 (3): 197-203
5. Fernandez-Jaen A, Fernandez-Mayoralas DM, Perez BC, et al. Atomoxetine for attention deficit hyperactivity disorder in mental retardation. Pediatr Neurol 2010; 43 (5): 341-7
6. Posey DJ, Wiegand RE, Wilkerson J, et al. Open-label atomoxetine for attention deficit/hyperactivity disorder symptoms associated with high-functioning pervasive developmental disorders. J Child Adolesc Psychopharmacol 2006; 16 (5): 599-610
7. Troost PW, Steenhuis MP, Tuyman-Qua HG, et al. Atomoxetine for attention-deficit/hyperactivity disorder symptoms in children with pervasive developmental disorders: a pilot study. J Child Adolesc Psychopharmacol 2006; 16 (5): 611-9
8. Arnold LE, Aman MG, Cook AM, et al. Atomoxetine for hyperactivity in autism spectrum disorders: placebo-controlled crossover pilot trial. J Am Acad Child Adolesc Psychiatry 2006; 45 (10): 1196-205
9. Kaufman J, Birmaher B, Brent D, et al. Schedule for Affective Disorders and Schizophrenia for School-Age Children-Present and Lifetime Version (K-SADS-PL): initial reliability and validity data. J Am Acad Child Adolesc Psychiatry 1997; 36: 980-8
10. Guy W, editor. ECDEU assessment manual for psychopharmacology: publication ADM 76-338. Washington, DC: US Department of Health, Education and Welfare, 1996: 218-22
11. Wechsler D. Wechsler intelligence scale for children, WISC-III. 3rd ed. New York (NY): Psychological Corporation, 1991
12. Swanson JM, Sandman CA, Deutsch C, et al. Methylphenidate hydrochloride given with or before breakfast: I. Behavioral, cognitive, and electrophysiologic effects. Pediatrics 1983; 72: 49-55
13. American Psychiatric Association. Diagnostic and statistical manual of mental disorders. 4th ed., text revision. Washington, DC: American Psychiatric Association, 2002
14. Aman MG, Buican B, Arnold LE. Methylphenidate treatment in children with borderline IQ and mental retardation: analysis of the three aggregated studies. J Child Adolesc Psychopharmacol 2003; 13: 28-40
15. Research Units on Pediatric Psychopharmacology (RUPP) Autism Network. Randomized, controlled, crossover trial of methylphenidate in pervasive developmental disorders with hyperactivity. Arch Gen Psychiatry 2005; 62: 1266-74
16. Handen BL, Breaux AM, Gosling A, et al. Efficacy of methylphenidate among mentally retarded children with attention deficit hyperactivity disorder. Pediatrics 1990; 86 (6): 922-30
17. Aman MG, Marks RE, Turbott SH, et al. Methylphenidate and thioridazine in the treatment of intellectually subaverage children: effects on cognitive-motor performance. J Am Acad Child Adolesc Psychiatry 1991; 30 (5): 816-24
18. Bymaster FP, Katner JS, Nelson DL, et al. Atomoxetine increases extracellular levels of norepinephrine and dopamine in prefrontal cortex of rat: a potential mechanism for efficacy in attention deficit/hyperactivity disorder. Neuropsychopharmacology 2002 Nov; 27 (5): 699-711
19. Diamond A. Consequences of variations in genes that affect dopamine in prefrontal cortex. Cereb Cortex 2007 Sep; 17 Suppl. 1: i161-70
20. Marshburn EC, Aman MG. Factor validity and norms for the aberrant behavior checklist in a community sample of children with mental retardation. J Autism Dev Disord 1992; 22: 357-73
21. Arnold LE, Vitiello B, McDougle C, et al. Parent-defined target symptoms respond to risperidone in RUPP autism study: customer approach to clinical trials. J Am Acad Child Adolesc Psychiatry 2003; 42: 1443-50

Correspondence: Dr *Luigi Mazzone*, Division of Child Neurology and Psychiatry, Department of Pediatrics, University of Catania, Via S. Sofia No. 78, Catania, 95100, Italy.
E-mail: gigimazzone@yahoo.it

CAMERA DEPUTATI - Allegato B

Seduta n. 494 del 30/6/2011

SALUTE

Interrogazione a risposta orale:

BINETTI. - *Al Ministro della salute*. - Per sapere - premesso che:
è in atto una intensa campagna pubblicitaria, a parere dell'interrogante e di esperti del settore, condotta con modalità non del tutto trasparenti, mirata all'inserimento di un nuovo psicofarmaco per bambini in Italia, di cui è ancora in corso la sperimentazione;
presso l'IRCCS Stella Maris di Pisa è, infatti, in corso una sperimentazione sulla Guanfacina;
nonostante esistano già altri due psicofarmaci per la sindrome da *deficit* di attenzione e iperattività (ADHD) regolarmente approvati in Italia, una delle agenzie di pubbliche relazioni della Shire, la Ketchum, starebbe conducendo una campagna per creare le condizioni per la migliore accettazione del farmaco nel nostro Paese, mediante il supporto all'organizzazione di convegni e seminari in cui si magnifica questo prodotto farmaceutico, sottolineando come l'assenza dello stesso dal mercato italiano creerebbe nocumento ad almeno 300.000 bambini che sarebbero in attesa di vederselo somministrare;
detta campagna di pubbliche relazioni potrebbe porsi in contrasto con l'articolo 6 del «Codice di condotta degli associati alla *Public Affairs Association*», gli articoli 5, 6 e 16 del codice di comportamento della Federazione relazioni pubbliche italiana e gli articoli 1 e 2 del Codice internazionale di Bruxelles per la condotta degli affari pubblici;
il registro per l'ADHD, utile strumento di monitoraggio anti-abuso istituito in forza della determinazione del 19 aprile 2007 dell'Agenzia italiana del farmaco pubblicata nella *Gazzetta Ufficiale* serie generale n. 95 del 24 aprile 2007 e gestito dall'Istituto superiore di sanità, ha visto un taglio graduale delle proprie spese di funzionamento da 150.000 euro l'anno del 2009 ad appena 30.000 euro l'anno del 2011, con serio pregiudizio al funzionamento dello stesso;
il consorzio interuniversitario non a scopo di lucro Cineca, che gestisce materialmente per conto dell'Istituto superiore di sanità il registro, con procedure di tutela dei dati dei bambini, è in arretrato di 2 anni nell'incasso del rimborso delle spese di gestione sostenute, ed entro il 31 dicembre 2011 interromperà quindi il servizio, obbligando così l'Istituto superiore di sanità a prendere in carico direttamente la complessa massa di informazioni, con un minore *standard* di sicurezza nel trattamento dei delicati dati sensibili sanitari dei bambini e le loro famiglie;
in caso di blocco delle attività del registro ADHD, si creerà pregiudizio grave al sistema di monitoraggio della somministrazione di questi psicofarmaci in Italia;
il «modello italiano» di sicurezza costituisce un'eccellenza assoluta nel mondo, in grado di garantire prescrizioni appropriate e non disinvolte di prodotti psicoattivi ai minori -:
quali iniziative urgenti intenda assumere il Ministro per garantire non solo la conferma dei fondi originariamente a disposizione dell'Istituto superiore di sanità per la gestione di questo progetto d'avanguardia, ma - come richiesto dallo stesso Istituto superiore di sanità - l'incremento degli stessi al fine di permettere l'inserimento nel registro di tutti gli psicofarmaci per l'età pediatrica, quali ad esempio quelli per gli episodi depressivi, somministrati in misura quindici volte superiore come quantità a quelli per l'iperattività e quindi richiedenti un'attenzione anche maggiore;
se sia vero che questa sperimentazione - della quale la casa farmaceutica produttrice non ha dato alcuna notizia pubblica, con riguardo alla salvaguardia del diritto alla salute dei bambini italiani - sia funzionale all'approvazione del farmaco per uso pediatrico e quindi all'inserimento di un terzo psicofarmaco per l'infanzia in Italia;
quali iniziative ritenga opportuno adottare tempestivamente per rinnovare il registro sull'ADHD,

utile strumento di controllo anti-abuso il cui decreto di funzionamento è scaduto e non rinnovato da mesi.
(3-01728)

Per ricevere la newsletter iscriversi al seguente indirizzo:
http://crc.marionegri.it/bonati/adhdnews/subscribe.html

ISTITUTO DI RICERCHE FARMACOLOGICHE MARIO NEGRI
DIPARTIMENTO DI SALUTE PUBBLICA
Laboratorio per la Salute Materno Infantile
Via Giuseppe La Masa, 19 - 20156 Milano MI - Italia - www.marionegri.it
tel +39 02 39014.511 - fax +39 02 3550924 - mother_child@marionegri.it