Attention Deficit Hyperactivity Disorder

ABSTRACTS

Arnold LE., 2001. Alternative treatments for adults with attention-deficit hyperactivity disorder
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Babcock Q., 2000. Student perceptions of methylphenidate abuse at a public liberal arts college.
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Alternative treatments for adults with attention-deficit hyperactivity disorder.

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Ann N Y Acad Sci 2001 Jun;931:310-41

A previous review of alternative treatments (Tx) of ADHD--those other than psychoactive medication and behavioral/psychosocial Tx--was supplemented with an ADDitional literature search focused on adults with ADHD. Twenty-four alternative Tx were identified, ranging in scientific documentation from discrediting controlled studies through mere hypotheses to positive controlled double-blind clinical trials. Many of them are applicable only to a specific subgroup. Although oligoantigenic (few-foods) diets have convincing double-blind evidence of efficacy for a properly selected subgroup of children, they do not appear promising for adults. Enzyme-potentiated desensitization, relaxation/EMG biofeedback, and deleading also have controlled evidence of efficacy. Iron supplementation, magnesium supplementation, Chinese herbals, EEG biofeedback, massage, meditation, mirror feedback, channel-specific perceptual training, and vestibular stimulation all have promising prospective pilot data, many of these tests reasonably controlled. Single-vitamin megadosage has some intriguing pilot trial data. Zinc supplementation is hypothetically supported by systematic case-control data, but no systematic clinical trial. Laser acupuncture has promising unpublished pilot data and may be more applicable to adults than children. Essential fatty acid supplementation has promising systematic case-control data, but clinical trials are equivocal. RDA vitamin supplementation, non-Chinese herbals, homeopathic remedies, and antifungal therapy have no systematic data in ADHD. Megadose multivitamin combinations are probably ineffective for most patients and are possibly dangerous. Simple sugar restriction seems ineffective. Amino acid supplementation is mildly effective in the short term, but not beyond 2-3 months. Thyroid treatment is effective in the presence of documented thyroid abnormality. Some alternative Tx of ADHD are effective or probably effective, but mainly for certain patients. In some cases, they are the Tx of choice, and initial evaluation should consider the relevant etiologies. A few have failed to prove effective in controlled trials. Most need research to determine whether they are effective and/or to define the applicable subgroup. Some of them, although not safer than standard Tx, may be preferable for an etiologic subgroup.

Does zinc moderate essential fatty acid and amphetamine treatment of attention-deficit/hyperactivity disorder?

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J Child Adolesc Psychopharmacol 2000 SUMMMER;10(2):111-7

Zinc is an important co-factor for metabolism relevant to neurotransmitters, fatty acids, prostaglandins, and melatonin, and indirectly affects dopamine metabolism, believed intimately involved in attention-deficit/hyperactivity disorder (ADHD). To explore the relationship of zinc nutrition to essential fatty acid supplement and stimulant effects in treatment of ADHD, we re-analyzed data from an 18-subject double-blind, placebo-controlled crossover treatment comparison of d-amphetamine and Efamol (evening primrose oil, rich in gamma-linolenic acid). Subjects were categorized as zinc-adequate (n = 5), borderline zinc (n = 5), and zinc-deficient (n = 8) by hair, red cell, and urine zinc levels; for each category, placebo-active difference means were calculated on teachers' ratings. Placebo-controlled d-amphetamine response appeared linear with zinc nutrition, but the relationship of Efamol response to zinc appeared U-shaped; Efamol benefit was evident only with borderline zinc. Placebo-controlled effect size (Cohen's d) for both treatments ranged up to 1.5 for borderline zinc and dropped to 0.3-0.7 with mild zinc deficiency. If upheld by prospective research, this post-hoc exploration suggests that zinc nutrition may be important for treatment of ADHD even by pharmacotherapy, and if Efamol benefits ADHD, it likely does so by improving or compensating for borderline zinc nutrition.

Student perceptions of methylphenidate abuse at a public liberal arts college.

Babcock Q, Byrne T. Massachusetts College of Liberal Arts, North Adams, USA.

J Am Coll Health 2000 Nov;49(3):143-5

With the ever-increasing diagnosis of attention deficit hyperactivity disorder, methylphenidate has become readily accessible in the college environment. Several properties of methylphenidate indicate abuse liability. A survey regarding the recreational use of methylphenidate was distributed to the student body at a public, liberal arts college. More than 16% of the students reported they had tried methylphenidate recreationally, and 12.7% reported they had taken the drug intranasally. Use of the drug was more common among traditional students than among nontraditional students. Among traditional-age students, reports of methylphenidate use were roughly equivalent to reports of cocaine and amphetamine use. Environmental conditions characteristic of college student life may influence the recreational use of the drug.

Longitudinal investigation of task persistence and sustained attention in children with prenatal cocaine exposure.

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Neurotoxicol Teratol 2001 Nov-Dec;23(6):545-59

The present study estimates the longitudinal effects of prenatal cocaine exposure on indicators of sustained attention processing at 3, 5 and 7 years of age in an urban sample of full-term African-American children (235 cocaine-exposed, 207 noncocaine-exposed). The sample was enrolled prospectively at birth, with documentation of prenatal drug exposure status through maternal interview, urine and meconium toxicology assays. Sustained attention was measured at age 3 years using a standardized measure of task persistence during a challenging task [G.A. Morgan, N.A. Busch-Rossnagel, C.A. Maslin-Cole and R.J. Harmon, Individualized Assessment of Mastery Motivation: Manual for 15-36 Month Old Children, 1992.], and at ages 5 and 7 years using omission error scores from computerized continuous performance tasks (CPT) [L. Greenberg, R. Leark, T. Dupuy, C. Corman, C. Kindschi, M. Cenedela, Test of Variables of Attention (T.O.V.A. and T.O.V.A.-A.), 22, Universal Attention Disorders, Los Alamitos, CA, 1996; C.K. Conners, Conners' Continuous Performance Test (CPT), second ed., Multi-Health Systems, Canada, 1995.]. Findings from longitudinal GLM/GEE analyses of the three measured time points support a stable influence of prenatal cocaine exposure on indicators of sustained attention, after controlling for prenatal exposure to alcohol, marijuana, tobacco and over 20 ADDitional medical and social-demographic covariates drawn from potentially confounding influences assessed at birth and later assessment visits (D=0.21; 95% CI=0.04, 0.38; P=.017). This effect was not mediated by fetal growth or gestational age and remained highly stable with increasing levels of covariate control. Separately, using the age 7 data, a structural equations model (SEM) was constructed combining all available self-report and bioassay data to measure magnitude of cocaine exposure in relationship to attention task performance. Results indicated a gradient of influence, with each standard deviation increase in the level of prenatal cocaine exposure relating to a 16% standard deviation increase in omission error scores at age 7. Overall findings support a stable cocaine-specific effect on indicators of sustained attention processing during the early childhood years. Results are discussed within the context of neurobiological and behavioral research linking prenatal cocaine exposure to long-lasting disruption of the brain systems subserving arousal and attention.

Relationships between serum-free fatty acids and zinc, and attention deficit hyperactivity disorder: a research note.

Bekaroglu M, Aslan Y, Gedik Y, Deger O, Mocan H, Erduran E, Karahan C. Department of Psychiatry, Technical University, Faculty of Medicine, Trabzon, Turkey.

J Child Psychol Psychiatry 1996 Feb;37(2):225-7

The purpose of this study is to evaluate the relationships between serum free fatty acids (FFA) and zinc, and attention deficit hyperactivity disorder (ADHD). Forty eight children with ADHD (33 boys, 15 girls) were included in the patient group and 45 healthy volunteer children (30 boys, 15 girls) constituted the control group. The mean serum FFA level in the patient group was 0.176 +/- 0.102 mEq/L and in control group, 0.562 +/- 0.225 mEq/L (< .001). The mean serum zinc level of patient group was 60.6 +/- 9.9 micrograms/dl and that of the control group, 105.8 +/- 13.2 micrograms/dl (< .001). A statistically significant correlation was found between zinc and FFA levels in the ADHD group. These findings indicate that zinc deficiency may play a role in aetiopathogenesis of ADHD. Although we observed decreased FFA levels in ADHD cases, it is necessary to determine whether this condition is a principal cause of ADHD or is secondary to zinc deficiency.

Attention deficit and infantile hyperactivity.

Berdonces JL. Universitat de Barcelona.

Rev Enferm 2001 Jan;24(1):11-4

Hyperactivity is a very common disorder in children (specially males) that today is considered as a clinical syndrome by scientific medicine. American Psychiatric Association establishes 10 symptoms to diagnose it, but they can be resumed in three characteristics: Impulsivity, Distraction, and Hyperactivity. There are different ways to treat it, but psychiatric medication has major risks in children. From complementary medicine we can find several aids in changing diet patterns and supplementing with vitamins or minerals. Chocolate, sugar, sweeteners, additives, preservatives, dyes, can enhance the incidence of this syndrome; instead the supplementation with lipids rich in PUFA's can prevent it. B complex vitamins, magnesium, copper, manganese or calcium can be interesting and in herbal medicine, sedative plants like passion flower, valerian or lemon balm are useful aids. Also liquorice, fennel and berries can be used for different physiological actions.

The effect of pyridoxine hydrochloride on blood serotonin and pyridoxal phosphate contents in hyperactive children.

Bhagavan HN, Coleman M, Coursin DB

Pediatrics 1975 Mar;55(3):437-41

The contents of serotonin (hydroxytryptamine) and pyridoxal phosphate (PLP) in the blood of 11 hyperactive children and 11 controls were determined on an outpatient basis. A significant decrease in serotonin content was found in blood samples from hyperactive patients as compared with controls. There were no differences in PLP content of blood between the two groups. Four children were selected for a study of the effects of pyridoxine hydrochloride (vitamin B6) on low serotonin levels. Oral doses of pyridoxine resulted in an appreciable increase in the serotonin content and a very large increase in the PLP content of blood in these hyperactive patients.

Non-stimulant treatments for ADHD.

Biederman J, Spencer T. Pediatric Psychopharmacology Unit, Massachusetts General Hospital, Boston, MA 02114, USA.

Eur Child Adolesc Psychiatry 2000;9 Suppl 1:I51-9

We reviewed the literature of medication trials in ADHD to evaluate the scope of the available non-stimulant treatments. A variety of compounds with a common noradrenergic/ dopaminergic activity have shown documented anti-ADHD activity. There is a substantial body of literature documenting the efficacy of tricyclic antidepressants on ADHD in over 1,000 subjects. In addition, the atypical antidepressant bupropion and the novel noradrenergic specific antidepressant tomoxetine have also been documented to be effective in the treatment of ADHD in controlled clinical trials. Despite wide use, the scientific base supporting the efficacy of alpha-2, noradrenergic agonists continues to be limited. Several lines of evidence provide preliminary support for the potential benefits of cholinergic cognitive enhancing drugs in such as anticholinesterase inhibitors (tacrine, donepezil) as well as novel nicotinic analogues (ABT-418). Despite these promising results, more research is needed on alternative pharmacologic treatments for the treatment of ADHD.

Foods and additives are common causes of the attention deficit hyperactive disorder in children.

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Ann Allergy 1994 May;72(5):462-8

The attention deficit hyperactive disorder (ADHD) is a neurophysiologic problem that is detrimental to children and their parents. Despite previous studies on the role of foods, preservatives and artificial colorings in ADHD this issue remains controversial. This investigation evaluated 26 children who meet the criteria for ADHD. Treatment with a multiple item elimination diet showed 19 children (73%) responded favorably, < .001. On open challenge, all 19 children reacted to many foods, dyes, and/or preservatives. A double-blind placebo controlled food challenge (DBPCFC) was completed in 16 children. There was a significant improvement on placebo days compared with challenge days (P = .003). Atopic children with ADHD had a significantly higher response rate than the nonatopic group. This study demonstrates a beneficial effect of eliminating reactive foods and artificial colors in children with ADHD. Dietary factors may play a significant role in the etiology of the majority of children with ADHD.

Psychostimulants in the treatment of children diagnosed with ADHD: risks and mechanism of action.

Breggin, P.R.

Int. J. Risk Safety Med. 1999; 12: 3-35.

No Abstract Available

Long-chain polyunsaturated fatty acids in children with attention-deficit hyperactivity disorder.

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Am J Clin Nutr 2000 Jan;71(1 Suppl):327S-30S

Attention-deficit hyperactivity disorder (ADHD) is the diagnosis used to describe children who are inattentive, impulsive, and hyperactive. ADHD is a widespread condition that is of public health concern. In most children with ADHD the cause is unknown, but is thought to be biological and multifactorial. Several previous studies indicated that some physical symptoms reported in ADHD are similar to symptoms observed in essential fatty acid (EFA) deficiency in animals and humans deprived of EFAs. We reported

previously that a subgroup of ADHD subjects reporting many symptoms indicative of EFA acid than did ADHD subjects with few such symptoms or control subjects. In another study using deficiency (L-ADHD) had significantly lower proportions of plasma arachidonic acid and docosahexaenoic contrast analysis of the plasma polar lipid data, subjects with lower compositions of total n-3 fatty acids had significantly more behavioral problems, temper tantrums, and learning, health, and sleep problems than did those with high proportions of n-3 fatty acids. The reasons for the lower proportions of long-chain polyunsaturated fatty acids (LCPUFAs) in these children are not clear; however, factors involving fatty acid intake, conversion of EFAs to LCPUFA products, and enhanced metabolism are discussed. The relation between LCPUFA status and the behavior problems that the children exhibited is also unclear. We are currently testing this relation in a double-blind, placebo-controlled intervention in a population of children with clinically diagnosed ADHD who exhibit symptoms of EFA deficiency.

On the role of cortical glutamate in obsessive-compulsive disorder and attention-deficit hyperactivity disorder, two phenomenologically antithetical conditions.

Carlsson ML. Department of Pharmacology, University of Goteborg, Sweden.

Acta Psychiatr Scand. 2000 Dec;102(6):401-13.

OBJECTIVE: The objective of the present study was to compare the phenomenology and pathophysiology of obsessive-compulsive disorder (OCD) and attention-deficit hyperactivity disorder/deficits in attention, motor control and perception (ADHD/DAMP).

METHOD: Through detailed studies of the literature on OCD and ADHD/DAMP the phenomenology of these two conditions is compared, and possible underlying pathophysiological mechanisms involving interactions between glutamate, dopamine, serotonin and acetylcholine are discussed, with emphasis on OCD. The present paper also discusses possible mechanisms of action for current pharmacological treatments of OCD and ADHD, as well as possible future treatment strategies for these disorders.

RESULTS: OCD and ADHD/DAMP are common neuropsychiatric conditions which in many regards appear to be each other's antipodes with respect to clinical manifestations, associated personality traits and brain biochemistry, notably prefrontal cortical glutamate activity. Future pharmacological treatments of these disorders may involve manipulations with glutamate, dopamine D1, serotonin 2A and nicotine receptors.

CONCLUSION: It appears that OCD is a hyperglutamatergic and ADHD a hypoglutamatergic condition, with prefrontal brain regions being especially affected.

The clinical role of computerized EEG in the evaluation and treatment of learning and attention disorders in children and adolescents.

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J Neuropsychiatry Clin Neurosci 2001 Spring;13(2):171-86

Quantitative EEG (QEEG) can play an important role in the evaluation and treatment of children and adolescents with attention deficit and learning disorders. Children with learning disorders are a heterogeneous population with QEEG abnormality in 25% to 45% of reported cases. EEG slowing is the most common abnormal finding, and the nature of the QEEG abnormality may be related to future academic performance. Children with attention disorders are a more homogeneous population, with QEEG abnormalities in up to 80%. In this population, frontal/polar regions are most likely to show deviations from normal development, with the thalamocortical and/or septal-hippocampal pathways most likely to be disturbed. QEEG shows high sensitivity and specificity for distinguishing normal children and children with learning disorders and attention disorders from each other and may provide useful information for determining the likelihood that children with attention problems will respond to treatment with stimulant medication.

Reward deficiency syndrome: genetic aspects of behavioral disorders.

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Prog Brain Res 2000;126:325-41

The dopaminergic and opioidergic reward pathways of the brain are critical for survival since they provide the pleasure drives for eating, love and reproduction; these are called 'natural rewards' and involve the release of dopamine in the nucleus accumbens and frontal lobes. However, the same release of dopamine and production of sensations of pleasure can be produced by 'unnatural

rewards' such as alcohol, cocaine, methamphetamine, heroin, nicotine, marijuana, and other drugs, and by compulsive activities such as gambling, eating, and sex, and by risk taking behaviors. Since only a minority of individuals become addicted to these compounds or behaviors, it is reasonable to ask what factors distinguish those who do become addicted from those who do not. It has usually been assumed that these behaviors are entirely voluntary and that environmental factors play the major role; however, since all of these behaviors have a significant genetic component, the presence of one or more variant genes presumably act as risk factors for these behaviors. Since the primary neurotransmitter of the reward pathway is dopamine, genes for dopamine synthesis, degradation, receptors, and transporters are reasonable candidates. However, serotonin, norepinephrine, GABA, opioid, and cannabinoid neurons all modify dopamine metabolism and dopamine neurons. We have proposed that defects in various combinations of the genes for these neurotransmitters result in a Reward Deficiency Syndrome (RDS) and that such individuals are at risk for abuse of the unnatural rewards. Because of its importance, the gene for the [figure: see text] dopamine D2 receptor was a major candidate gene. Studies in the past decade have shown that in various subject groups the Taq I A1 allele of the DRD2 gene is associated with alcoholism, drug abuse, smoking, obesity, compulsive gambling, and several personality traits. A range of other dopamine, opioid, cannabinoid, norepinephrine, and related genes have since been added to the list. Like other behavioral disorders, these are polygenically inherited and each gene accounts for only a small per cent of the variance. Techniques such as the Multivariate Analysis of Associations, which simultaneously examine the contribution of multiple genes, hold promise for understanding the genetic make up of polygenic disorders.

Can what a child eats make him dull, stupid or hyperactive?

Crook WG.

J Learn Disabil 1980 May;13(5):281-6

No Abstract Available

Getting the attention you need.

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Harv Bus Rev. 2000 Sep-Oct;78(5):118-26, 200.

Employees have an enormous amount of business information at their fingertips--more specifically, at their desktops. The floodgates are open; profitable possibilities abound. But having to handle all that information has pushed downsized staffs to the brink of an acute attention deficit disorder. To achieve corporate goals, business leaders need their employees' full attention--and that attention is in short supply. Authors Thomas Davenport and John Beck have studied how companies manage the attention of their employees and their site visitors. In this article, they analyze the components of attention management through three lenses--economic, psychobiological, and technological--and offer guidelines for keeping employees focused on crucial corporate tasks. Their lessons are drawn from the best practices employed by today's stickiest Web sites and by traditional attention industries such as advertising, film, and television. The authors say executives must manage attention knowing that it's a zero-sum game (there's only so much to go around). Managers should also consider capitalizing on the basic survival and competitive instincts we all have that help determine how much attention we pay to certain things. For instance, the threat of corporate demise--and the consequent loss of jobs and livelihoods--undoubtedly focuses workers' attention on the need to change. Likewise, internal competition among business units may give employees added incentive to pay attention to a profit or sales goal. Leaders today need to pay more attention to attention because it's widely misunderstood and widely mismanaged, the authors conclude.

Bupropion sustained release in adolescents with comorbid attention-deficit/hyperactivity disorder and depression.

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J Am Acad Child Adolesc Psychiatry 2001 Mar;40(3):307-14

OBJECTIVE: To determine whether bupropion sustained release (SR) is effective and well-tolerated in adolescents with comorbid attention-deficit/hyperactivity disorder (ADHD) and depression.

METHOD: Subjects were 24 adolescents (aged 11-16 years old) with ADHD and either major depressive disorder or dysthymic disorder. After a 2-week, single-blind placebo lead-in, subjects were treated for 8+ weeks with bupropion SR at doses flexibly titrated up to 3 mg/kg b.i.d. (mean final doses: 2.2 mg/kg q A.M. and 1.7 mg/kg q P.M.). Outcomes were global improvement in ADHD and depression (clinician-rated), along with changes in depressive symptomatology (parent- and child-rated), ADHD symptomatology (parent- and teacher-rated), and functional impairment (parent-rated).

RESULTS: Clinicians rated 14 subjects (58%) responders in both depression and ADHD, 7 (29%) responders in depression only, and 1 (4%) a responder in ADHD only. Compared with post-placebo ratings, final parents' (< .0005) and children's (p = .016) ratings of depressive symptomatology improved significantly, as did parents' (< .0005) but not teachers' (p = .080) ratings of ADHD symptomatology. Final ratings of functional impairment improved significantly from enrollment (< .0005). No subject discontinued medication because of side effects.

CONCLUSIONS: Bupropion SR may be effective and well-tolerated in adolescents with comorbid ADHD and depressive disorders. However, randomized, placebo-controlled studies are needed.

DMAE. Smart Drugs and Nutrients 1990.

Dean, J., Morgenthaler, J.

Menlo Park, CA: Health Freedom Publications.

Prior stimulant treatment in adolescents with bipolar disorder: association with age at onset.

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Bipolar Disord 2001 Apr;3(2):53-7

OBJECTIVES: To compare demographic and clinical characteristics between bipolar adolescents with and without a history of stimulant treatment, we hypothesized that adolescents treated with stimulants would have an earlier age at onset of bipolar disorder, independent of co-occurring attention-deficit-hyperactivity disorder (ADHD).

METHOD: Thirty-four adolescents hospitalized with mania were assessed using the Washington University at St Louis Kiddie Schedule for Affective Disorders and Schizophrenia (WASH-U-KSADS). We systematically evaluated age at onset of bipolar disorder and pharmacological treatment history.

RESULTS: Bipolar adolescents with a history of stimulant exposure prior to the onset of bipolar disorder had an earlier age at onset of bipolar disorder than those without prior stimulant exposure. Additionally, bipolar adolescents treated with at least two stimulant medications had a younger age at onset compared with those who were treated with one stimulant. There was no difference in age at onset of bipolar disorder between bipolar adolescents with and without ADHD.

CONCLUSIONS: Our results suggest that stimulant treatment, independent of ADHD, is associated with younger age at onset of bipolar disorder. A behavioral sensitization model is proposed to explain our findings. There are several limitations to our study including the small sample size, the retrospective assessment of stimulant exposure and age at onset of bipolar disorder, and the inclusion of only hospitalized patients, who may be more likely to present with a severe illness. Nonetheless, future prospective longitudinal investigations that systematically assess the effects of stimulant medications in children with or at genetic risk for bipolar disorder are warranted.

Controlled trial of oligoantigenic treatment in the hyperkinetic syndrome.

Egger J, Carter CM, Graham PJ, Gumley D, Soothill JF.

Lancet 1985 Mar 9;1(8428):540-5

76 selected overactive children were treated with an oligoantigenic diet, 62 improved, and a normal range of behaviour was achieved in 21 of these. Other symptoms, such as headaches, abdominal pain, and fits, also often improved. 28 of the children who improved completed a double-blind, crossover, placebo-controlled trial in which foods thought to provoke symptoms were reintroduced. Symptoms returned or were exacerbated much more often when patients were on active material than on placebo. 48 foods were incriminated. Artificial colorants and preservatives were the commonest provoking substances, but no child was sensitive to these alone.

Child maltreatment, other trauma exposure, and posttraumatic symptomatology among children with oppositional defiant and attention deficit hyperactivity disorders.

Ford JD, Racusin R, Ellis CG, Daviss WB, Reiser J, Fleischer A, Thomas J. Center for the Study of High Utilizers of Health Care, University of Connecticut School of Medicine, USA.

Child Maltreat 2000 Aug;5(3):205-17

Consecutive child psychiatric outpatient admissions with disruptive behavior or adjustment disorders were assessed by validated instruments for trauma exposure and posttraumatic stress disorder (PTSD) symptoms and other psychopathology. Four reliably diagnosed groups were defined in a retrospective case-control design: Attention Deficit Hyperactivity Disorder (ADHD), Oppositional Defiant Disorder (ODD), comorbid ADHD-ODD, and adjustment disorder controls. ODD and (although to a lesser extent) ADHD were associated with a history of physical or sexual maltreatment. PTSD symptoms were most severe if (a) ADHD and maltreatment co-occurred or (b) ODD and accident/illness trauma co-occurred. The association between ODD and PTSD Criterion D (hyperarousal/hypervigilance) symptoms remained after controlling for overlapping symptoms, but the association of ADHD with PTSD symptoms was largely due to an overlapping symptom. These findings suggest that screening for maltreatment, other trauma, and PTSD symptoms may enhance prevention, treatment, and research concerning childhood disruptive behavior disorders.

Psychosocial functioning in a prepubertal and early adolescent bipolar disorder phenotype.

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J Am Acad Child Adolesc Psychiatry 2000 Dec;39(12):1543-8

OBJECTIVE: To compare psychosocial functioning (PF) in a prepubertal and early adolescent bipolar disorder phenotype (PEA-BP) sample to two comparison groups, i.e., attention-deficit/hyperactivity disorder (ADHD) and community controls (CC).

METHOD: There were 93 PEA-BP (with or without comorbid ADHD), 81 ADHD, and 94 CC subjects who were participants in an ongoing study, the Phenomenology and Course of Pediatric Bipolar Disorders. Cases in the PEA-BP and ADHD groups were outpatients obtained by consecutive new case ascertainment, and CC subjects were from a survey conducted by the Research Triangle Institute. To fit the study phenotype, PEA-BP subjects needed to have current DSM-IV mania or hypomania with elation and/or grandiosity as one criterion. Assessments for PF were by experienced research nurses who were blind to group status. Mothers and children were separately interviewed with the Psychosocial Schedule for School Age Children-Revised.

RESULTS: Compared with both ADHD and CC subjects, PEA-BP cases had significantly greater impairment on items that assessed maternal-child warmth, maternal-child and paternal-child tension, and peer relationships.

CONCLUSIONS: Clinicians need to consider PF deficits when planning interventions. In the PEA-BP group, there was a 43% rate of hypersexuality with < 1% rate of sexual abuse, supporting hypersexuality as a manifestation of child mania.

Blunted catecholamine responses after glucose ingestion in children with attention deficit disorder.

Girardi NL, Shaywitz SE, Shaywitz BA, Marchione K, Fleischman SJ, Jones TW, Tamborlane WV. Department of Pediatrics, Yale University School of Medicine, New Haven, Connecticut 06510, USA.

Pediatr Res 1995 Oct;38(4):539-42

Eating simple sugars has been suggested as having adverse behavioral and cognitive effects in children with attention deficit disorder (ADD), but a physiologic mechanism has not been established. To address this issue, metabolic, hormonal, and cognitive responses to a standard oral glucose load (1.75 g/kg) were compared in 17 children with ADD and 11 control children. Baseline and oral glucose-stimulated plasma glucose and insulin levels were similar in both groups, including the nadir glucose level 3-5 h after oral glucose (3.5 +/- 0.2 mmol/L in ADD and 3.3 +/- 0.2 mmol/L in control children). The late glucose fall stimulated a rise in plasma epinephrine that was nearly 50% lower in ADD than in control children (1212 +/- 202 pmol/L versus 2228 +/- 436 pmol/L, < 0.02). Plasma norepinephrine levels were also lower in ADD than in control children, whereas growth hormone and glucagon concentrations did not differ between the groups. Matching test scores were lower and reaction times faster in ADD than in control children before and after oral glucose, and both groups showed a deterioration on the continuous performance test in association with the late fall in glucose and rise in epinephrine. These data suggest that children with ADD have a general impairment of sympathetic activation involving adrenomedullary as well as well as central catecholamine regulation.

Perceived passage of time: its possible relationship to attention-deficit hyperactivity disorder.

Goddard J. Preventive Medicine, The University of Mississippi Medical Center, Jackson, Mississippi, USA.

Med Hypotheses 2000 Oct;55(4):351-2

Previous studies have shown that various factors may affect the perceived passage of time. Even boredom is thought to be related to a perception of time passing slowly. There might be an inverse relationship between brain processing speed and perceived time passage such that a slow processing speed would yield a fast perception of time passage. This could relate to attention-deficit hyperactivity disorder (ADHD) - it could be caused by a distorted sense of time in which time passes so quickly that concentration becomes difficult. Under this model, stimulants would be a logical therapy for ADHD patients. Copyright 2000 Harcourt Publishers Ltd.

Gabapentin and methylphenidate treatment of a preadolescent with attention deficit hyperactivity disorder and bipolar disorder.

Hamrin V, Bailey K. Yale University, School of Nursing, New Haven, Connecticut 06510, USA.

J Child Adolesc Psychopharmacol 2001 Fall;11(3):301-9

Gabapentin is an anticonvulsant drug released in the United States in 1993 for use as adjunctive therapy in refractory partial epilepsy. The mechanism of action of gabapentin is unknown, but the drug has very favorable pharmacokinetics and a good safety profile, which allows its use in high-risk patients. Several reports have described the successful use of gabapentin for bipolar disorders in adults, but there are no controlled studies in the use of gabapentin in children and adolescents. We describe a 12-year-old boy with a history of attention deficient hyperactivity disorder (ADHD), reading disorder, mixed receptive and expressive language disorder, encopresis, and bipolar disorder II who was treated with gabapentin 200 mg/day added to methylphenidate 30 mg/day. Within 3 weeks the improvement and stabilization of mood symptoms was remarkable, as noted by mother, teacher, and clinician, and remained so for 6 months of follow-up. Comorbid bipolar disorder and ADHD is a hotly debated topic in the child and adolescent psychiatric literature, with rates of comorbid ADHD and bipolar disorder ranging from 22% to 90%. Controlled studies are needed to evaluate the possible antimanic mood stabilizing and/or antidepressant properties or gabapentin in youths.

The influence of soy-derived phosphatidylserine on cognition in age-associated memory impairment.

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Nutr Neurosci 2001;4(2):121-34

Phosphatidylserine (PS) is a phospholipid widely sold as a nutritional supplement. PS has been claimed to enhance neuronal membrane function and hence cognitive function, especially in the elderly. We report the results of a clinical trial of soybean-derived PS (S-PS) in aging subjects with memory complaints. Subjects were 120 elderly (< 57 years) of both sexes who fulfilled the more stringent criteria for age-associated memory impairment (AAMI); some also fulfilled the criteria for age-associated cognitive decline. Subjects were allocated at random to one of the three treatment groups: placebo, 300mg S-PS daily, or 600mg S-PS daily. Assessments were carried out at baseline, after 6 and 12 weeks of treatment, and after a wash-out period of 3 weeks. Tests of learning and memory, choice reaction time, planning and attentional functions were administered at each assessment. Delayed recall and recognition of a previously learned word list comprised the primary outcome measures. No significant differences were found in any of the outcome variables between the treatment groups. There were also no significant interactions between treatment and 'severity of memory complaints'. In conclusion, a daily supplement of S-PS does not affect memory or other cognitive functions in older individuals with memory complaints.

Hypothalamic-pituitary-adrenal axis function in children with attention-deficit hyperactivity disorder.

Kaneko M, Hoshino Y, Hashimoto S, Okano T, Kumashiro H. Department of Neuropsychiatry, Fukushima Medical College, Japan.

J Autism Dev Disord 1993 Mar;23(1):59-65

Examined hypothalamic-pituitary-adrenal axis (HPA axis) function in 30 children with attention-deficit hyperactivity disorder (ADHD) by measuring the diurnal variation and response to the dexamethasone suppression test (DST) of saliva cortisol. Normal diurnal saliva cortisol rhythm was found in only 43.3% of the ADHD children. DST showed suppression in 46.7% of the ADHD children. An abnormal diurnal rhythm and nonsuppression to the DST were more frequent in the severely hyperactive group than in the mildly were more frequent in the severely hyperactive group than in the mildly hyperactive group of children with ADHD. These results suggest abnormalities in HPA axis function in some children with ADHD, especially those exhibiting severe hyperactivity.

No association between CHRNA7 microsatellite markers and attention-deficit hyperactivity disorder.

Kent L, Green E, Holmes J, Thapar A, Gill M, Hawi Z, Fitzgerald M, Asherson P, Curran S, Mills J, Payton A, Craddock N.

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Am J Med Genet 2001 Dec 8;105(8):686-9

Attention-deficit hyperactivity disorder (ADHD) is a highly heritable, common psychiatric disorder of childhood that probably involves several genes. There are several lines of evidence suggesting that the nicotinic system may be functionally significant in ADHD. First, nicotine promotes the release of dopamine and has been shown to improve attention in adults with ADHD, smokers, and nonsmokers. Second, ADHD is a significant risk factor for early initiation of cigarette smoking in children and maternal cigarette smoking appears to be a risk factor for ADHD. Finally, animal studies in rats and monkeys also suggest that nicotine may be involved in attentional systems and locomotor activity. The nicotinic system has previously been studied in schizophrenia where the neuronal nicotinic acetylcholine receptor alpha 7 subunit gene (CHRNA7) has been implicated in decreased P50 inhibition and attentional disturbances in patients with schizophrenia and in many of their nonschizophrenic relatives. Three known microsatellite markers (D15S165, D15S1043, and D15S1360) near the nicotinic acetylcholine alpha 7 receptor gene, CHRNA7, were studied in 206 ADHD parent-proband trios of children aged 5-16 with ADHD according to DSM-IV criteria. Children with known major medical or psychiatric conditions or mental retardation (< 70) were excluded from the study. Markers D15S165 and D15S1360 were in linkage disequilibrium. The extended Transmission Disequilibrium Test analyses demonstrated no evidence that variation at the microsatellite markers D15S1360, D15S1043, and D15S165 influences susceptibility to ADHD. However, it remains possible that the CHRNA7 gene and other nicotinic system genes may be involved in conferring susceptibility to ADHD. Copyright 2001 Wiley-Liss, Inc.

Attention deficit/hyperactivity disorder (ADHD) in children: rationale for its integrative management.

Kidd PM.

Altern Med Rev 2000 Oct;5(5):402-28

Attention Deficit/Hyperactivity Disorder (ADHD) is the most common behavioral disorder in children. ADHD is characterized by attention deficit, impulsivity, and sometimes overactivity ("hyperactivity"). The diagnosis is empirical, with no objective confirmation available to date from laboratory measures. ADHD begins in childhood and often persists into adulthood. The exact etiology is unknown; genetics plays a role, but major etiologic contributors also include adverse responses to food additives, intolerances to foods, sensitivities to environmental chemicals, molds, and fungi, and exposures to neurodevelopmental toxins such as heavy metals and organohalide pollutants. Thyroid hypofunction may be a common denominator linking toxic insults with ADHD symptomatologies. Abnormalities in the frontostriatal brain circuitry and possible hypofunctioning of dopaminergic pathways are apparent in ADHD, and are consistent with the benefits obtained in some instances by the use of methylphenidate (Ritalin) and other potent psychostimulants. Mounting controversy over the widespread use of methylphenidate and possible life-threatening effects from its long-term use make it imperative that alternative modalities be implemented for ADHD management. Nutrient deficiencies are common in ADHD; supplementation with minerals, the B vitamins (added in singly), omega-3 and omega-6 essential fatty acids, flavonoids, and the essential phospholipid phosphatidylserine (PS) can ameliorate ADHD symptoms. When individually managed with supplementation, dietary modification, detoxification, correction of intestinal dysbiosis, and other features of a wholistic/integrative program of management, the ADHD subject can lead a normal and productive life.

Methylphenidate increased regional cerebral blood flow in subjects with attention deficit/hyperactivity disorder.

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Yonsei Med J 2001 Feb;42(1):19-29

The regional cerebral blood flow (rCBF) responses to methylphenidate (MPH) treatment were examined in children with attention deficit/hyperactivity disorder (ADHD). Thirty-two male children, diagnosed with ADHD by the DSM-IV diagnostic criteria, other behavioral assessment scales and neuropsychological battery, were studied using 99mTc-HMPAO-single photon emission computed tomography (SPECT). Subjects were studied before and after MPH treatment. First, using an image subtraction method, we obtained a NDR parametric image of each patient and found increased cerebral blood flow in the frontal lobes, caudate nuclei and thalamic areas after treatment. When the changes in SPECT and clinical response were compared, the matching rate, sensitivity and specificity between them were found to be 77.1, 80.0 and 79.2%, respectively. Second, three transaxial brain slices delineating anatomically defined regions of interest (ROI) at 20, 40, and 60mm above the orbitomeatal line (OML) were used, with the average number of counts for each region of interest normalized to the area of the cerebellar maximal uptake. The left and right prefrontal areas, and caudate and thalamic areas showed significant increases in rCBF after MPH treatment. These findings suggested MPH could affect the function of the fronto-striato-thalamic circuit, which is known as the pathophysiologic site of ADHD and could be used to correct the underlying brain dysfunction of ADHD.

Functioning, comorbidity and treatment of 141 adults with attention deficit hyperactivity disorder (ADHD) at a psychiatric

outpatient department. [Article in Dutch]

Kooij JJ, Aeckerlin LP, Buitelaar JK. GGZ Delfland, polikliniek Psychiatrie, Reinier de Graafweg 3-11, 2625 AD Delft.

Ned Tijdschr Geneeskd 2001 Aug 4;145(31):1498-501

OBJECTIVE: To describe the functioning, comorbidity and treatment of adults with attention deficit hyperactivity disorder (ADHD). DESIGN: Retrospective.

METHOD: In the period 1 May 1995 to 31 January 1998, 141 patients aged 18-54 were diagnosed with ADHD at the Delfland Psychiatric Outpatients' Department, Delft, the Netherlands. For all of these patients, data concerning the functioning, comorbidity, and the response to treatment with clonidine (n = 34) or methylphenidate (n = 99), were collected from anamneses, hetero-anamneses and school reports.

RESULTS: The most frequent complaints were: mood-swings, rage-outbursts, sensation-seeking behaviour, sleeping disorders, anxiety and depressive symptoms. In 94% (n = 123) of the cases, childhood onset of ADHD symptoms was confirmed by a family member. The distribution of ADHD subtypes was comparable to the distribution in children. Psychiatric comorbidity was common. Treatment with methylphenidate was more effective and better tolerated than treatment with clonidine.

CONCLUSION: With respect to ADHD subtypes, patterns of comorbidity and effectiveness of medication, ADHD in the adults studied was comparable with what is known about ADHD in children.

Brief video-assisted observation of visual attention, facial expression, and motor skills for diagnosis of attention deficit/hyperactivity disorder (ADHD). [Article in German]

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Prax Kinderpsychol Kinderpsychiatr 2001 Oct;50(8):607-21

Can video assisted observation of visual attention, facial expression and motor skills contribute to the diagnosis of attention deficit/hyperactivity disorder (ADHD)? 20 children from 6 to 10 years of age, diagnosed for ADHD following the DSM-IV criteria, and an age and sex matched control group of 20 children with harmless upper airway infections were filmed during 3 minutes playing cards with their mothers and 7 minutes of oral arithmetic exercises. Two persons were trained for eight hours in recognizing 22 signs for visual attention loss, alterated facial expression like oversized and sustained smile and abnormal motor skills in ADHD-patient videos. Then they viewed minutes 2 and 3 and 3 and 4 of the 40 children in a randomized sequence and scored the signs. 8 of the 22 signs showed high (< .75) and 9 showed medium (< .6) interrater correlations. The presence of signs in the ADHD and in the control group was highly significantly different (a = 0.01, U-Test of Mann and Whitney) for 10 of the 22 signs and significantly different for other 4 signs (a = 0.05). The four field table comparison between the frequency of the signs showed correct positioning in 80% of all cases. The loss of visual attention was the most frequent sign in ADHD children. The signs of alterated facial expression werealso among the highly correlated signs. These are used by us to find theindividual dose for stimulant medication.

Effects of chronic nicotine and methylphenidate in adults with attention deficit/hyperactivity disorder.

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Exp Clin Psychopharmacol 2001 Feb;9(1):83-90

Acute nicotine treatment has been found to reduce symptoms of attention deficit/hyperactivity disorder in adults (E. D. Levin, C. K. Conners, et al., 1996). In this study, chronic nicotine effects were compared with placebo and methylphenidate. Acute and chronic nicotine treatment significantly attenuated the rise in hit reaction time standard error over session blocks on the Conners Continuous Performance Test (C. K. Conners et al., 1996). Acute nicotine significantly reduced severity of clinical symptoms on the Clinical Global Impressions scale (National Institute of Mental Health, 1985). Nicotine caused a significant decrease in self-report of depressive mood as measured by the Profile of Mood States test (D. M. McNair, M. Lorr, & L. F. Droppleman, 1981). This small study (40 participants) provided evidence that nicotine treatment can reduce severity of attentional deficit symptoms and produce improvement on an objective computerized attention task.

Herbs of activating blood circulation to remove blood stasis.

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Clin Hemorheol Microcirc 2000;23(2-4):127-31

Drugs with the efficacy of modifying rheological properties of blood, blood vessels and their interactions are denoted by "hemorheologicals". Drugs of anti-hyperviscosemia, anti-coagulants, anti-platelet drugs, anti-thrombotics, vasodilators, endothelial cell protectors and anti-arthrosclerosis should be considered as hemorheologicals due to the actions in keeping blood fluidity and in maintaining normal vascular functions. The studies in hemorheology indicate that a tendency of hyperviscosity, hypercoagulation and being prone to thrombosis is prevalent in the elderly. Hemorheologicals are importance for and aging and life-threatening diseases. Blood stasis syndrome is a common pathological syndrome in the elderly. In traditional Chinese medicine, the treatment for the syndrome is by herbs which activates blood circulation to remove blood stasis. The herbs have the efficacy of improving hemorheological events. Therefore, the herbs are the source for developing hemorheologicals. Ligustrazine isolated from Chuangxiong is an example. It showed significant inhibition on shear induced platelet aggregation and on platelet intracellular calcium demonstrated by laser confocal microscope.

Effect of the herbal extract combination Panax quinquefolium and Ginkgo biloba on attention-deficit hyperactivity disorder: a pilot study.

Lyon MR, Cline JC, Totosy de Zepetnek J, Shan JJ, Pang P, Benishin C. Oceanside Functional Medicine Research Institute, Nanaimo, BC.

J Psychiatry Neurosci 2001 May;26(3):221-8

OBJECTIVE: A combination herbal product containing American ginseng extract, Panax quinquefolium, (200 mg) and Ginkgo biloba extract (50 mg) (AD-FX; CV Technologies, Edmonton, Alta.) was tested for its ability to improve the symptoms of attention-deficit hyperactivity disorder (ADHD).

DESIGN: Open study.

PATIENTS: 36 children ranging in age from 3 to 17 years who fit the diagnostic criteria for ADHD.

INTERVENTIONS: AD-FX capsules were taken twice a day on an empty stomach for 4 weeks. Patients were instructed not to change any other medications during the study.

OUTCOME MEASURES: At the beginning of the study, after 2 weeks, and then at the end of the 4-week trial, parents completed the Conners' Parent Rating Scale--revised, long version, a questionnaire that assesses a broad range of problem behaviours (and was used as an indication of ADHD symptom severity).

RESULTS: After 2 weeks of treatment, the proportion of the subjects exhibiting improvement (i.e., decrease in T-score of at least 5 points) ranged from 31% for the anxious-shy attribute to 67% for the psychosomatic attribute. After 4 weeks of treatment, the proportion of subjects exhibiting improvement ranged from 44% for the social problems attribute to 74% for the Conners' ADHD index and the DSM-IV hyperactive-impulsive attribute. Five (14%) of 36 subjects reported adverse events, only 2 of which were considered related to the study medication.

CONCLUSIONS: These preliminary results suggest AD-FX treatment may improve symptoms of ADHD and should encourage further research on the use of ginseng and Ginkgo biloba extracts to treat ADHD symptoms.

Long-term prognosis in attention-deficit/hyperactivity disorder.

Mannuzza S, Klein RG. New York University Child Study Center, New York, USA.

Child Adolesc Psychiatr Clin N Am 2000 Jul;9(3):711-26

The authors have traced the developmental course of ADHD from childhood to adulthood, showing that it is a bumpy road for many. In early and middle adolescence, relative deficits are seen in academic and social functioning, ADHD symptoms remain problematic in two thirds to three quarters of these children, and antisocial behaviors, in some cases amounting to CD, are common. Many of these same difficulties persist into the late teenage years. Deficits continue to be observed in academic and social domains (compared with controls, probands exhibit lower grades, more courses failed, worse performance on standardized tests, have fewer friends, and are rated less adequate in psychosocial adjustment). About two fifths continue to experience ADHD symptoms to a clinically significant degree. One quarter to one third have a diagnosed antisocial disorder, and two thirds of these individuals are arrested. Also, drug abuse is observed in a significant minority of these youths. Importantly, the greatest risk factor for the development of antisocial behavior and substance abuse by the late teenage years is the maintenance of ADD symptoms. When

evaluated in their mid-twenties, dysfunctions are apparent in these same areas. Compared with controls, probands complete less schooling, hold lower-ranking occupations, and continue to suffer from poor self-esteem and social skills deficits. In addition, significantly more probands than controls exhibit an antisocial personality and, perhaps, a substance use disorder in adulthood. Furthermore, many do not outgrow all facets of their childhood syndrome. These relative deficits, however, do not tell the whole story of the ADHD child's adult fate. Indeed, nearly all probands were gainfully employed. Furthermore, some had achieved a higher-level education (e.g., completed Master's degree, enrolled in medical school) and occupation (e.g., accountant, stock broker). In addition, a full two thirds of these children showed no evidence of any mental disorder in adulthood. In conclusion, although ADHD children, as a group, fare poorly compared with their non-ADHD counterparts, the childhood syndrome does not preclude attaining high educational and vocational goals, and most children no longer exhibit clinically significant emotional or behavioral problems once they reach their mid-twenties.

Atomoxetine in the treatment of children and adolescents with attention-deficit/hyperactivity disorder: a randomized, placebo-controlled, dose-response study.

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Pediatrics 2001 Nov;108(5):E83

OBJECTIVE: Atomoxetine is an investigational, nonstimulant pharmacotherapy being studied as potential treatment for attention-deficit/hyperactivity disorder (ADHD). It is thought to act via blockade of the presynaptic norepinephrine transporter in the brain. We assessed the efficacy of 3 doses of atomoxetine compared with placebo in children and adolescents with ADHD.

METHODS: A total of 297 children and adolescents who were 8 to 18 years of age and had ADHD as defined by the Diagnostic and Statistical Manual of Mental Disorders, 4th edition, were randomized to placebo or atomoxetine dosed on a weight-adjusted basis at 0.5 mg/kg/day, 1.2 mg/kg/day, or 1.8 mg/kg/day for an 8-week period. ADHD symptoms, affective symptoms, and social and family functioning were assessed using parent and investigator rating scales.

RESULTS: Approximately 71% of children enrolled were male, approximately 67% met criteria for mixed subtype (both inattentive and hyperactive/impulsive symptoms), and the only common psychiatric comorbidity was oppositional defiant disorder (approximately 38% of the sample). At baseline, symptom severity was rated as moderate to severe for most children. At endpoint, atomoxetine 1.2 mg/kg/day and 1.8 mg/kg/day were consistently associated with superior outcomes in ADHD symptoms compared with placebo and were not different from each other. The dose of 0.5 mg/kg/day was associated with intermediate efficacy between placebo and the 2 higher doses, suggesting a graded dose-response. Social and family functioning also were improved in the atomoxetine groups compared with placebo with statistically significant improvements in measures of children's ability to meet psychosocial role expectations and parental impact. Discontinuations as a result of adverse events were < 5% for all groups.

CONCLUSION: Among children and adolescents aged 8 to 18, atomoxetine was superior to placebo in reducing ADHD symptoms and in improving social and family functioning symptoms. Atomoxetine was associated with a graded dose-response, and 1.2 mg/kg/day seems to be as effective as 1.8 mg/kg/day and is likely to be the appropriate initial target dose for most patients. Treatment with atomoxetine was safe and well tolerated.

Serotonin and aggression in children.

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Curr Psychiatry Rep 2000 Apr;2(2):95-101

Research consistently indicates that in animals and adults, reduced central serotonergic (5-HT) function is associated with increased aggression. This relationship has been elucidated via cerebrospinal fluid monoamine metabolite levels, hormonal responses to pharmacologic challenge using serotonergic probes, platelet receptor binding studies, and, more recently, through molecular genetic approaches. In contrast, studies examining the relationship of 5-HT to aggression in children have been characterized by inconsistent findings. The literature examining the relationship between central 5-HT function and aggression is reviewed. Several hypotheses that might account for the discrepancies in the child literature are examined.

Food intakes of U.S. children and adolescents compared with recommendations.

Munoz KA, Krebs-Smith SM, Ballard-Barbash R, Cleveland LE. Applied Research Branch, Division of Cancer Prevention and Control, National Cancer Institute, National Institutes of Health, Bethesda, Maryland, USA.

Pediatrics. 1997 Sep;100(3 Pt 1):323-9

OBJECTIVES: To determine the proportion of youth meeting national recommendations for food group intake and to identify food intake patterns.

DESIGN: The US Department of Agriculture's 1989-1991 Continuing Surveys of Food Intakes by Individuals were used to estimate food intake. Intake was determined from 3 days of diet by disaggregating foods into their component ingredients and using weights that correspond to servings.

PARTICIPANTS: The sample included 3307 youth, 2 to 19 years of age, living in the 48 conterminous United States. Main Outcome Measures. Mean number of servings and percentage of individuals meeting national recommendations for food group intake according to demographic characteristics, patterns of intake, and nutrient profiles associated with each pattern.

RESULTS: Mean numbers of servings per day were below minimum of youth meeting recommendations ranged from approximately 30% for fruit, grain, meat, and dairy to 36% for vegetables. Sixteen percent of youth did not meet any recommendations, and 1% met recommendations for all food groups except the dairy group (ages 2 to 11). Percentages all recommendations. The pattern of meeting all recommendations resulted in nutrient intakes above the recommended dietary allowances and was high in fat. Conversely, meeting none of the recommendations resulted in intakes well below the recommended dietary allowances for some nutrients. Total fat and added sugars averaged 35% and 15% of energy, respectively, and levels were similar among most demographic groups.

CONCLUSION: Children and teens in the United States follow eating patterns that do not meet national recommendations. Nutrition education and intervention are needed among US children.

Mercury amalgam toxicity.

O'Brien, J. Ft. Lauderdale, FL: Life Extension Foundation. http://www.lef.org/magazine/mag2001/may2001_report_mercury_1.html

Life Extension Magazine 2001 May; 7(5): 43-51.

Distributed grey and white matter deficits in hyperkinetic disorder: MRI evidence for anatomical abnormality in an attentional network.

Overmeyer S, Bullmore ET, Suckling J, Simmons A, Williams SC, Santosh PJ, Taylor E. Institute of Psychiatry and Guy's, King's and St Thomas's School of Medicine, London.

Psychol Med 2001 Nov;31(8):1425-35

BACKGROUND: Previous neuroimaging studies of children with attention deficit hyperactivity disorder (ADHD) have demonstrated anatomic and functional abnormalities predominantly in frontal and striatal grey matter. Here we report the use of novel image analysis methods, which do not require prior selection of regions of interest, to characterize distributed morphological deficits of both grey and white matter associated with ADHD.

METHODS: Eighteen children with a refined phenotype of ADHD, who also met ICD-10 criteria for hyperkinetic disorder (mean age 10.4 years), and 16 normal children (mean age 10.3 years) were compared using magnetic resonance imaging. The groups were matched for handedness, sex, height, weight and head circumference. Morphological differences between groups were estimated by fitting a linear model at each voxel in standard space, applying a threshold to the resulting voxel statistic maps to generate clusters of spatially contiguous suprathreshold voxels, and testing cluster 'mass', or the sum of suprathreshold voxel statistics in each 2D cluster, by repeated random resampling of the data.

RESULTS: The hyperkinetic children had significant grey matter deficits in right superior frontal gyrus (Brodmann area (BA) 8/9), right posterior cingulate gyrus (BA 30) and the basal ganglia bilaterally (especially right globus pallidus and putamen). They also demonstrated significant central white matter deficits in the left hemisphere anterior to the pyramidal tracts and superior to the basal ganglia.

CONCLUSIONS: This pattern of spatially distributed grey matter deficit in the right hemisphere is compatible with the hypothesis that ADHD is associated with disruption of a large scale neurocognitive network for attention. The left hemispheric white matter deficits may be due to dysmyelination.

Attention deficit/hyperactivity disorder: characteristics, interventions and models.

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Neurotoxicol Teratol 2000 Sep-Oct;22(5):631-51

An epidemiological study of Attention Deficit/Hyperactivity Disorder (ADHD) suggests that the prevalence may be two to three times higher than the figure of 3-5% often cited. In addition, the data suggest that both underdiagnosis and overdiagnosis occur frequently. Rodent animal models of ADHD, like the Spontaneously Hypertensive Rat (SHR) and other rat models such as those with chemical and radiation-induced brain lesions and cerebellar stunting, and the Coloboma mouse model exhibit clear similarities with several aspects of the human disorder and should prove useful in studying specific traits. Operant behavioral tasks that model learning, short-term memory and simple discriminations are sensitive to ADHD and methylphenidate has been shown to normalize ADHD performance in a short-term memory task. Recent findings challenge not only the current postulate that response inhibition is a unique deficit in ADHD, but also the concepts of ADHD and its treatment, which presume intact perceptual abilities. Time perception deficits may account, in part, for the excessive variability in motor response times on speeded reaction time tasks, motor control problems and motor clumsiness associated with ADHD. The Multimodality Treatment Study of ADHD (MTA) provided data suggesting that pharmacological interventions that included systematic and frequent follow-up with parents and teachers, with or without psychosocial interventions, are superior to psychosocial interventions or standard community care alone. Additionally, the MTA was one of the first studies to demonstrate benefits of multimodal and pharmacological interventions lasting longer than 1 year. Imaging studies have demonstrated differences in brain areas in children with ADHD: anterior corpus callosum, right anterior white matter, and cerebellar volumes are all decreased in children with ADHD and there is less brain asymmetry in ADHD subjects. Additionally, functional imaging studies, coupled with pharmacological manipulations, suggest decreased blood flow and energy utilization in prefrontal cortex and striatum and the dysregulation of catecholamine systems in persons with ADHD.

Physicians' Desk Reference 2002.

PDR. Adderall.

Montvale, NJ: Medical Economics/Simon & Schuster.

Attention-deficit hyperactivity disorder and vulnerability to the development of alcoholism: use of the Wender-Utah Rating Scale for retrospective diagnostic of ADHD in the childhood of alcoholic patients. [Article in Spanish]

Ponce Alfaro G, Rodriguez-Jimenez Caumel R, Perez Rojo JA, Monasor Sanchez R, Rubio Valladolid G, Jimenez Arriero MA, Palomo Alvarez T. Unidad de Conductas Adictivas (UCA), Hospital Universitario Doce de Octubre.

Actas Esp Psiquiatr. 2000 Nov-Dec;28(6):357-66.

In the last years, it has been accumulated data about an important association between addictions and attention-deficit hyperactivity disorder (ADHD). Both disorders share clinic aspects and relevant biological markers, and for both it has been postulated alterations in the same cerebral systems.

OBJECTIVE: To evaluate the rate of possible ADHD in the early ages of adult alcoholic patients, in contrast with controls.

METHOD: It was realized an adaptation of Wender-Utah Rating Scale (WURS) and it was analyzed its psychometric characteristics. It was administered to 117 alcoholic patients and to 52 controls.

RESULTS: The mean score of WURS is significatively higher in alcoholic group than in the control one (32.26 vs. 16.55, < 0.0001). The percentage of alcoholic patients who has a score upper the different cut-off points (36 and 46) is also higher in alcoholic group than in the control one (36.75% vs 7.69%; < 0.0005; 18.8% vs. 1.92%; < 0.01, respectively). The mean score is higher in alcoholics with other comorbid addiction than in alcoholics without it (37.61 vs. 29.17; < 0.018), and is higher in alcoholic patients who usually have intoxicated states in an high-moderate grade than those who have it in a low-nule one.

CONCLUSIONS: Among alcoholic patients exists an important group with high scores in the WURS, it could indicate high rates of ADHD in early ages. It was discused the clinic and etiopathogenetics implications, and the convenience of advancing in the developemnt of diagnostic tools.

Natural outcome of ADHD with developmental coordination disorder at age 22 years: a controlled, longitudinal, community-based study.

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J Am Acad Child Adolesc Psychiatry 2000 Nov;39(11):1424-31

OBJECTIVE: There is a need for controlled longitudinal studies in the field of attention disorders in the general population.

METHOD: In a community-based follow-up study, 55 of 61 subjects aged 22 years, who had attention-deficit/hyperactivity disorder (ADHD) with and without comorbid developmental coordination disorder (DCD) at initial workup at age 7 years, were compared, on a multitude of outcome variables, with 46 of 51 age-matched subjects without such diagnoses. None of the subjects had received stimulant treatment. Psychiatrists performing the follow-up study were blind to original diagnostic group status.

RESULTS: In the ADHD/DCD group 58% had a poor outcome compared with 13% in the comparison group (< .001). Remaining symptoms of ADHD, antisocial personality disorder, alcohol abuse, criminal offending, reading disorders, and low educational level were overrepresented in the ADHD/DCD groups. The combination of ADHD and DCD appeared to carry a particularly gloomy outlook.

CONCLUSIONS: Childhood ADHD and DCD appears to be a most important predictor of poor psychosocial functioning in early adulthood. It would seem appropriate to screen for such disorders in schools and clinics so that therapies may be started early.

Parallels between attention deficit hyperactivity disorder and behavioral deficits produced by neurotoxic exposure in monkeys.

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Environ Health Perspect. 2000 Jun;108 Suppl 3:405-8.

Attention deficit hyperactivity disorder (ADHD) is a disability that affects between 3 and 7% of children, with a significant number of individuals continuing to be affected into adolescence and adulthood. ADHD is characterized in part by an inability to organize complex sequences of behavior, to persist in the face of distracting stimuli, and to respond appropriately to the consequences of past behavior. There are some parallels between the features of ADHD and the behavior of monkeys exposed developmentally to lead or polychlorinated biphenyls (PCBs), as evidenced by research from our laboratory. Both lead and PCB exposure produce deficits on discrimination reversal and spatial delayed alternation performance; treated monkeys exhibit deficits in their ability to change an already established response strategy and inhibit inappropriate responses. Monkeys exposed developmentally to lead or PCBs also perform differently from control monkeys on a fixed interval schedule of reinforcement, which requires the temporal organization of behavior using only internal cues. Whereas the etiology of ADHD is multifactorial, the possibility that neurotoxic agents in the environment contribute to the incidence of ADHD warrants attention.

The potential role of fatty acids in attention-deficit/hyperactivity disorder.

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Prostaglandins Leukot Essent Fatty Acids 2000 Jul-Aug;63(1-2):79-87

As currently defined, attention-deficit/hyperactivity disorder (ADHD) encompasses a broad constellation of behavioural and learning problems and its definition and diagnosis remain controversial. The aetiology of ADHD is acknowledged to be both complex and multifactorial. The proposal considered here is that at least some features of ADHD may reflect an underlying abnormality of fatty acid metabolism. Clinical and biochemical evidence is discussed which suggests that a functional deficiency of certain long-chain polyunsaturated fatty acids could contribute to many of the features associated with this condition. The implications in terms of fatty acid treatment proposals are also discussed; such a form of treatment is relatively safe compared to existing pharmacological interventions, although further studies are still needed in order to evaluate its potential efficacy in the management of ADHD symptoms. Copyright 2000 Harcourt Publishers Ltd.

A randomized double-blind, placebo-controlled study of the effects of supplementation with highly unsaturated fatty acids on ADHD-related symptoms in children with specific learning difficulties.

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Prog Neuropsychopharmacol Biol Psychiatry 2002 Feb;26(2):233-9

(1) The authors tested the prediction that relative deficiencies in highly unsaturated fatty acids (HUFAs) may underlie some of the

behavioral and learning problems associated with attention-deficit/hyperactivity disorder (ADHD) by studying the effects of HUFA supplementation on ADHD-related symptoms in children with specific learning difficulties (mainly dyslexia) who also showed ADHD features. (2) Forty-one children aged 8-12 years with both specific learning difficulties and above-average ADHD ratings were randomly allocated to HUFA supplementation or placebo for 12 weeks. (3) At both baseline and follow-up, a range of behavioral and learning problems associated with ADHD was assessed using standardized parent rating scales. (4) At baseline, the groups did not differ, but after 12 weeks mean scores for cognitive problems and general behavior problems were significantly lower for the group treated with HUFA than for the placebo group; there were significant improvements from baseline on 7 out of 14 scales for active treatment, compared with none for placebo. Group differences in change scores all favored HUFA, reaching conventional significance levels for 3 out of 14 scales. (5) HUFA supplementation appears to reduce ADHD-related symptoms in children with specific learning difficulties. Given the safety and tolerability of this simple treatment, results from this pilot study strongly support the case for further investigations.

Synthetic food coloring and behavior, a dose response effect in a double-blind, placebo controlled, repeated-measures study.

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J Pediatr 1994 Nov;125(5 Pt 1):691-8

OBJECTIVE: To establish whether there is an association between the ingestion of synthetic food colorings and behavioral change in children referred for assessment of "hyperactivity."

PARTICIPANTS: From approximately 800 children referred to the Royal Children's Hospital (Melbourne) for assessment of suspected hyperactivity, 200 were included in a 6-week open trial of a diet free of synthetic food coloring. The parents of 150 children reported behavioral improvement with the diet, and deterioration on the introduction of foods noted to contain synthetic coloring. A 30-item behavioral rating inventory was devised from an examination of the clinical histories of 50 suspected reactors. Thirty-four other children (23 suspected reactors, 11 uncertain reactors) and 20 control subjects, aged 2 to 14 years, were studied.

DESIGN: A 21-day, double-blind, placebo-controlled, repeated-measures study used each child as his or her own control. Placebo, or one of six dose levels of tartrazine (1, 2, 5, 10, 20, 50 mg), was administered randomly each morning, and behavioral ratings were recorded by parents at the end of each 24 hours.

RESULTS: The study identified 24 children as clear reactors (19 of 23 "suspected reactors," 3 of 11 "uncertain reactors," and 2 of 20 "control subjects"). They were irritable and restless and had sleep disturbance. Significant reactions were observed at all six dose levels. A dose response effect was obtained. With a dose increase greater than 10 mg, the duration of effect was prolonged.

CONCLUSION: Behavioral changes in irritability, restlessness, and sleep disturbance are associated with the ingestion of tartrazine in some children. A dose response effect was observed.

ADHD: making the appropriate pediatric assessment.

Sangare J.

Lippincotts Prim Care Pract. 2000 Mar-Apr;4(2):193-206

Attention deficit/hyperactivity disorder (ADHD) is a term used to describe a constellation of inappropriate levels of inattention and impulsivity. The history of name changes from minimal brain syndrome, to hyperkinetic syndrome, to what is now known as ADHD, reflects the influence of neurology, pediatrics, and psychiatry. This "evolutionary" process has been replete with controversy stemming from the diverse views of broad disciplines that have attempted to define its range, scope, and treatment. ADHD has been defined within a "neurobiopyschoeducational" context, which has made the diagnosis and treatment of this disorder more challenging. The aim of this article is to highlight the current revisions to the ADHD DSM-IV diagnostic criteria and to identify current assessment issues and strategies to aid in making the proper diagnosis and treatment plan.

The effect of vitamin-mineral supplementation on juvenile delinquency among American schoolchildren: a randomized, double-blind placebo-controlled trial.

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J Altern Complement Med 2000 Feb;6(1):7-17

CONTEXT: Numerous studies conducted in juvenile correctional institutions have reported that violence and serious antisocial behavior have been cut almost in half after implementing nutrient-dense diets that are consistent with the World Health Organization's guidelines for fats, sugar, starches, and protein ratios. Two controlled trials tested whether the cause of the behavioral improvements was psychological or biological in nature by comparing the behavior of offenders who either received placebos or vitamin-mineral supplements designed to provide the micronutrient equivalent of a well-balanced diet. These randomized trials reported that institutionalized offenders, aged 13 to 17 years or 18 to 26 years, when given active tablets produced about 40% less violent and other antisocial behavior than the placebo controls. However, generalization could not be made to typical schoolchildren without a controlled trial examining violence and antisocial behavior in public schools.

OBJECTIVES: To determine if schoolchildren, aged 6 to 12 years, who are given low dose vitamin-mineral tablets will produce significantly less violence and antisocial behavior in school than classmates who are given placebos.

DESIGN: A stratified randomized, double-blind, placebo-controlled trial with pretest and post-test measures of antisocial behavior on school property.

SETTINGS AND SUBJECTS: Two "working class," primarily Hispanic elementary schools in Phoenix, Arizona. Approximately half of the potential schoolchildren participated, i.e., 468 students aged 6 to 12 years.

INTERVENTION: Daily vitamin-mineral supplementation at 50% of the U.S. recommended daily allowance (RDA) for 4 months versus placebo. The supplement was designed to raise vitamin-mineral intake up to the levels currently recommended by the National Academy of Sciences for children aged 6 to 11 years.

OUTCOME MEASURE: Violent and nonviolent delinquency as measured by official school disciplinary records.

RESULTS: Of the 468 students randomly assigned to active or placebo tablets, the 80 who were disciplined at least once between September 1st and May 1st served as the research sample. During intervention, the 40 children who received active tablets were disciplined, on average, 1 time each, a 47% lower mean rate of antisocial behavior than the 1.875 times each for the 40 children who received placebos (95% confidence interval, 29% to 65%, < 5 .020). The children who took active tablets produced lower rates of antisocial behavior in 8 types of recorded infractions: threats/fighting, vandalism, being disrespectful, disorderly conduct, defiance, obscenities, refusal to work or serve, endangering others, and nonspecified offenses.

CONCLUSION: Poor nutritional habits in children that lead to low concentrations of water-soluble vitamins in blood, impair brain function and subsequently cause violence and other serious antisocial behavior. Correction of nutrient intake, either through a well-balanced diet or low-dose vitamin-mineral supplementation, corrects the low concentrations of vitamins in blood, improves brain function and subsequently lowers institutional violence and antisocial behavior by almost half. This paper adds to the literature by enabling previous research to be generalized from older incarcerated subjects with a history of antisocial behavior to a normal population of younger children in an educational setting.

Effect of early marasmic malnutrition on subsequent physical and psychological development. Malnutrition, Learning and Behavior Behavoir

Schrimshaw, S., Gordon, J.E.

1968. Cambridge, MA: MIT Press.

Study on the Effects of Super Blue Green Algae

Sevulla, I., Aguiree, N.

1995. Managua, Nicaragua: Universidad Centro Americano.

Effect of interactive metronome training on children with ADHD.

Shaffer RJ, Jacokes LE, Cassily JF, Greenspan SI, Tuchman RF, Stemmer PJ Jr. College of Human Medicine, Michigan State University, Ann Arbor, USA.

Am J Occup Ther 2001 Mar-Apr;55(2):155-62

OBJECTIVE: The purpose of this study was to determine the effects of a specific intervention, the Interactive Metronome, on selected aspects of motor and cognitive skills in a group of children with attention deficit hyperactivity disorder (ADHD).

METHOD: The study included 56 boys who were 6years to 12 years of age and diagnosed before they entered the study as having ADHD. The participants were pretested and randomly assigned to one of three matched groups. A group of 19 participants receiving 15 hr of Interactive Metronome training exercises were compared with a group receiving no intervention and a group receiving training on selected computer video games.

RESULTS: A significant pattern of improvement across 53 of 58 variables favoring the Interactive Metronome treatment was found. Additionally, several significant differences were found among the treatment groups and between pretreatment and posttreatment factors on performance in areas of attention, motor control, language processing, reading, and parental reports of improvements in regulation of aggressive behavior.

CONCLUSION: The Interactive Metronome training appears to facilitate a number of capacities, including attention, motor control, and selected academic skills, in boys with ADHD.

The effects of magnesium physiological supplementation on hyperactivity in children with attention deficit hyperactivity disorder (ADHD). Positive response to magnesium oral loading test.

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Magnes Res 1997 Jun;10(2):149-56

Children with ADHD are 'a group at risk' as far as their further emotional and social development and educational possibilities are concerned, and the consequences of the lack of an appropriate therapy appears to be serious. Some of these children do not respond to prevailing therapy methods. It is reported that dietetic factors can play a significant role in the etiology of ADHD syndrome, and magnesium deficiency can help in revealing hyperactivity in children. The aim of our work was to assess the influence of magnesium supplementation on hyperactivity in patients with ADHD. The examination comprised 50 hyperactive children, aged 7-12 years, who fulfilled DSM IV criteria for ADHD syndrome, with recognized deficiency of magnesium in the blood (blood serum and red blood cells) and in hair using atomic absorption spectroscopy. In the period of 6 months those examined regularly took magnesium preparations in a dose of about 200 mg/day. 30 of those examined with ADHD showed coexisting disorders specific to developmental age, and 20 of them showed disruptive behaviour. The control group consisted of 25 children with ADHD and magnesium deficiency, who were treated in a standard way, without magnesium preparations. 15 members of this group showed coexisting disorders specific for developmental age, and 10 members showed disruptive behaviour. Hyperactivity was assessed with the aid of psychometric scales: the Conners Rating Scale for Parents and Teachers, Wender's Scale of Behavior and the Quotient of Development to Freedom from Distractibility. In the group of children given 6 months of magnesium supplementation, independently of other mental disorders coexisting with hyperactivity, an increase in magnesium contents in hair and a significant decrease of hyperactivity of those examined has been achieved, compared to their clinical state before supplementation and compared to the control group which had not been treated with magnesium.

Analysis of neurosteroid levels in attention deficit hyperactivity disorder.

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Int J Neuropsychopharmacol 2001 Sep;4(3):259-64

Neurosteroids are important neuroactive substrates with demonstrated involvement in several neurophysiological and disease processes. Attention deficit hyperactivity disorder (ADHD) has been associated with dysregulation of the catecholaminergic and serotonergic systems, however its relationship to irregularities or changes in neurosteroid levels remains unknown. We examined the relationship between blood levels of dehydroepiandrosterone (DHEA), its principal precursor pregnenolone and its principal metabolite dehydroepiandrosterone sulphate (DHEAS) in 29 young male subjects aged 7-15 years with DSM-IV criteria of ADHD. Subjects were evaluated by a specially designed scale, following which patients were divided into two groups according to severity of symptomatology. Results indicated significant inverse correlations between clinical symptomatology and levels of DHEA and pregnenolone in the total group. These inverse correlations were particularly evident in the less severe group of subjects. Levels of DHEA and DHEAS were inversely correlated with the hyperactivity subscale. Furthermore, using median blood levels as a cut-off indicator, higher blood levels of DHEA and DHEAS were associated with fewer ADHD symptoms, in particular hyperactivity symptomatology. Our findings suggest a possible protective effect of various neurosteroids on the expression of ADHD symptomatology.

Linkage of the dopamine D4 receptor gene and attention deficit/hyperactivity disorder.

Sunohara GA, Roberts W, Malone M, Schachar RJ, Tannock R, Basile VS, Wigal T, Wigal SB, Schuck S, Moriarty J, Swanson JM, Kennedy JL, Barr CL. Neurogenetics Section, The Centre for Addiction and Mental Health, Toronto, Ontario, Canada.

J Am Acad Child Adolesc Psychiatry 2000 Dec;39(12):1537-42

OBJECTIVE: There is considerable evidence supporting a genetic component in the etiology of attention-deficit/hyperactivity disorder (ADHD). Because stimulant medications act primarily on the dopaminergic system, dopamine system genes are prime candidates for genetic susceptibility factors for ADHD. Previous studies by several groups have observed a significant association of ADHD and an allele with 7 copies of the 48 base pair repeat in the third exon of the dopamine D4 receptor.

METHOD: The authors sought to replicate these previous findings by collecting an independent sample of families from Toronto, Ontario, Canada, and confirming this finding in an expanded sample of ADHD families collected from Irvine, California. Using the transmission disequilibrium test (TDT), the authors tested for biased transmission of the 7-repeat allele at the exon III polymorphism of the dopamine D4 receptor locus in these samples of ADHD subjects.

RESULTS: Biased transmission of the 7-repeat allele from parents to ADHD probands and their affected siblings was observed in the 2 new samples of families collected in Toronto and Irvine (TDT chi2 = 2.711, 1 df, one-sided p value = .050) and for these samples combined with the 52 families previously reported from Irvine (TDT chi2 = 6.426, 1 df, one-sided p value = .006).

CONCLUSIONS: The results of this study further support the possibility of a role of the dopamine D4 receptor locus in ADHD.

The effects of exercise on children with attention-deficit hyperactivity disorder.

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Med Sci Sports Exerc 2002 Feb;34(2):203-12

PURPOSE: The effects of exercise on children with attention-deficit hyperactivity disorder (ADHD) were evaluated by studying the rate of spontaneous eye blinks, the acoustic startle eye blink response (ASER), and motor impersistence among 8- to 12-yr-old children (10 boys and 8 girls) meeting DSM-lll-R criteria for ADHD.

METHODS: Children ceased methylphenidate medication 24 h before and during each of three daily conditions separated by 24-48 h. After a maximal treadmill walking test to determine cardiorespiratory fitness (VO(2peak)), each child was randomly assigned to counterbalanced conditions of treadmill walking at an intensity of 65-75% VO(2peak) or quiet rest. Responses were compared with a group of control participants (11 boys and 14 girls) equated with the ADHD group on several key variables.

RESULTS: Boys with ADHD had increased spontaneous blink rate, decreased ASER latency, and decreased motor impersistence after maximal exercise. Girls with ADHD had increased ASER amplitude and decreased ASER latency after submaximal exercise.

CONCLUSIONS: The findings suggest an interaction between sex and exercise intensity that is not explained by physical fitness, activity history, or selected personality attributes. The clinical meaning of the eye blink results is not clear, as improvements in motor impersistence occurred only for boys after maximal exercise. Nonetheless, these preliminary findings are sufficiently positive to encourage additional study to determine whether a session of vigorous exercise has efficacy as a dopaminergic adjuvant in the management of behavioral features of ADHD.

Efficacy of modafinil compared to dextroamphetamine for the treatment of attention deficit hyperactivity disorder in adults.

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J Child Adolesc Psychopharmacol. 2000 Winter;10(4):311-20.

Our objective was to compare the efficacy of the new wake-promoting drug modafinil to that of dextroamphetamine for the treatment of attention deficit hyperactivity disorder (ADHD) in adults. Twenty-two adults who met DSM-IV criteria for ADHD participated in a randomized, double-blind, placebo-controlled, three-phase crossover study comparing placebo, modafinil, and dextroamphetamine for the treatment of ADHD. The twice-daily study medications were titrated to doses of optimum efficacy over 4-7 days and then held constant during the rest of each 2-week treatment phase. Measures of improvement included the DSM-IV ADHD Behavior Checklist for Adults, the Controlled Oral Word Association Test (COWAT, using the letters C, F, and L version), Stroop, and Digit Span (Wechsler Adult Intelligence Scale version). For the 21 (96%) completers, the mean (+/- SD) optimum doses of modafinil and dextroamphetamine were 206.8 mg/day +/- 84.9 and 21.8 mg/day +/- 8.9, respectively. Scores on the DSM-IV ADHD Checklist (< 0.001) were significantly improved over the placebo condition following treatment with both active medications. Performance on the COWAT (< 0.05) reached trend levels of significance. Both medications were generally well tolerated. This preliminary study suggests that modafinil may be a viable alternative to conventional stimulants for the treatment of adults with ADHD.

Is attention-deficit/hyperactivity disorder an energy deficiency syndrome?

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Biol Psychiatry 2001 Aug 1;50(3):151-8

Attention-deficit/hyperactivity disorder (ADHD) is a highly heritable yet clinically heterogeneous syndrome associated with hypocatecholamine function in subcortical and prefrontal cortical regions and clinical response to medications that enhance catecholamine function. The goal of this article is to present a hypothesis about the etiology of ADHD by synthesizing these findings with recent experiments indicating that activity-dependent neuronal energy consumption is regulated by cortical astrocytes. The scientific literature was searched from 1966 to the present using MEDLINE and relevant key words. Inattention and impulsivity may be related to hypofunctionality of catecholamine projection pathways to prefrontal cortical areas, resulting in decreased neuronal energy availability. This may be mediated by astrocyte catecholamine receptors that normally regulate energy availability during neuronal activation. At least some forms of ADHD may be viewed as cortical, energy-deficit syndromes secondary to catecholamine-mediated hypofunctionality of astrocyte glucose and glycogen metabolism, which provides activity-dependent energy to cortical neurons. Several tests of this hypothesis are proposed.

Spirulina maxima prevents induction of fatty liver by carbon tetrachloride in the rat.

Torres-Duran PV, Miranda-Zamora R, Paredes-Carbajal MC, Mascher D, Diaz-Zagoya JC, Juarez-Oropeza MA. Departamento de Bioquimica, UNAM, Mexico, D.F., Mexico.

Biochem Mol Biol Int. 1998 Apr;44(4):787-93

The aim of the present work was to assess the capacity of Spirulina maxima to prevent fatty liver development induced in rats by an intraperitoneal single dose (1 ml/kg) of carbon tetrachloride. Liver and serum lipids were quantified two or four days after treatment with this agent. Liver lipid concentration did not differ in rats fed on a purified diet with or without Spirulina. However, after carbon tetrachloride treatment, liver triacylglycerols were significantly lower in rats fed on a diet with Spirulina 5% than in rats without Spirulina in their diet (< 0.05). Furthermore, the increased liver cholesterol values, induced by carbon tetrachloride treatment, were not observed in rats that received Spirulina. These results support the potential hepatoprotective role of Spirulina.

Hepatoprotective effect of C-phycocyanin: protection for carbon tetrachloride and R-(+)-pulegone-mediated hepatotoxicity in rats.

Vadiraja BB, Gaikwad NW, Madyastha KM. Department of Organic Chemistry, Indian Institute of Science, Bangalore, 560 012, India.

Biochem Biophys Res Commun. 1998 Aug 19;249(2):428-31.

Effect of C-phycocyanin (from Spirulina platensis) pretreatment on carbontetrachloride and R-(+)-pulegone-induced hepatotoxicity in rats was studied. Intraperitoneal (i.p.) administration (200 mg/kg) of a single dose of phycocyanin to rats, one or three hours prior to R-(+)-pulegone (250 mg/kg) or carbontetrachloride (0.6 ml/kg) challenge, significantly reduced the hepatotoxicity caused by these chemicals. For instance, serum glutamate pyruvate transaminase (SGPT) activity was almost equal to control values. The losses of microsomal cytochrome P450, glucose-6-phosphatase and aminopyrine-N-demethylase were significantly reduced, suggesting that phycocyanin provides protection to liver enzymes. It was noticed that the level of menthofuran, the proximate toxin of R-(+)-pulegone was nearly 70% more in the urine samples collected from rats treated with R-(+)-pulegone alone than rats treated with the combination of phycocyanin and R-(+)-pulegone. The possible mechanism involved in the hepatoprotection is discussed.

Pay attention: ritalin acts much like cocaine.

Vastag B.

JAMA. 2001 Aug 22-29;286(8):905-6

No Abstract Available

A randomized, double-blind, placebo-controlled trial of docosahexanoic acid supplementation in children with attention-deficit/hyperactivity disorder.

Voigt RG, Llorente AM, Jensen CL, Fraley JK, Berretta MC, Heird WC. Division of Developmental and Behavioral Pediatrics, Mayo Clinic, Rochester, Minnesota 55905, USA.

J Pediatr. 2001 Aug;139(2):189-96.

OBJECTIVE: To determine whether docosahexaenoic acid (DHA) supplementation for 4 months decreases the symptoms of attention-deficit/hyperactivity disorder (ADHD).

STUDY DESIGN: Sixty-three 6- to-12-year-old children with ADHD, all receiving effective maintenance therapy with stimulant medication, were assigned randomly, in a double-blind fashion, to receive DHA supplementation (345 mg/d) or placebo for 4 months. Outcome variables included plasma phospholipid fatty acid patterns, scores on laboratory measures of inattention and impulsivity (Test of Variables of Attention, Children's Color Trails test) while not taking stimulant medication, and scores on parental behavioral rating scales (Child Behavior Checklist, Conners' Rating Scale). Differences between groups after 4 months of DHA supplementation or placebo administration were determined by analysis of variance, controlling for age, baseline value of each outcome variable, ethnicity, and ADHD subtype.

RESULTS: Plasma phospholipid DHA content of the DHA-supplemented group was 2.6-fold higher at the end of the study than that of the placebo group (4.85 +/- 1.35 vs 1.86 +/- 0.87 mol % of total fatty acids; < 001). Despite this, there was no statistically significant improvement in any objective or subjective measure of ADHD symptoms.

CONCLUSION: A 4-month period of DHA supplementation (345 mg/d) does not decrease symptoms of ADHD.

Effects of sugar on aggressive and inattentive behavior in children with attention deficit disorder with hyperactivity and normal children.

Wender EH, Solanto MV. Schneider Children's Hospital, Long Island Jewish Medical Center, New Hyde Park, New York 11042.

Pediatrics. 1991 Nov;88(5):960-6

Foods high in refined sugar are claimed to exacerbate hyperactivity and increase aggressive behavior. Controlled studies have failed to confirm any effect on hyperactivity and effects on inattention have been equivocal. Possible effect on aggressive behavior has received little study. This study assessed cognitive attention and aggressive behavior immediately following an acute ingestion of sugar compared with saccharin and aspartame-sweetened placebos in 17 subjects with attention deficit disorder with hyperactivity compared with 9 age-matched control subjects. The sugar and placebo challenges were given with a breakfast high in carbohydrate. Although the children with attention deficit disorder with hyperactivity were significantly more aggressive than the control subjects, there were no significant effects of sugar or either placebo on the aggressive behavior of either group. However, inattention, as measured by a continuous performance task, increased only in the attention deficit disorder with hyperactivity group following sugar, but not saccharin or aspartame. This result is of questionable clinical significance inasmuch as aggressive behavior was unchanged. The finding may be due to the combination of the sugar challenge with a high-carbohydrate breakfast. These findings should be replicated and any possible clinical significance should be documented before any dietary recommendations can be made.

Adults with ADHD. An overview.

Wender PH, Wolf LE, Wasserstein J. Department of Psychiatry, University of Utah School of Medicine, Salt Lake City, Utah 84132, USA.

Ann N Y Acad Sci. 2001 Jun;931:1-16

Attention-Deficit Hyperactivity Disorder (ADHD) is a common, genetically transmitted neurological disorder, with onset in childhood, probably mediated by decreased brain dopaminergic functioning. The first author was one of the earliest to describe the persistence of symptoms into adulthood. Prevalence and natural history data suggest that of the 3 to 10% of children diagnosed with ADHD, one- to two-thirds (somewhere between 1 and 6% of the general population) continue to manifest appreciable ADHD symptoms into adult life. This paper describes how ADHD in adults can be readily diagnosed and treated, despite resembling or coexisting with other psychiatric disorders. The Wender Utah diagnostic criteria address adult characteristics of the disorder. Informant and patient interviews and rating scales are used to determine the psychiatric status of the patient as a child, make a retroactive diagnosis of childhood ADHD, and establish the current diagnosis of the adult. Stringent diagnosis is key to determining effective treatment. Dopamine agonist stimulant medications appear to be the most effective in treating ADHD. About 60% of patients receiving stimulant medication showed moderate-to-marked improvement, as compared with 10% of those receiving placebo. The core symptoms of hyperactivity, inattention, mood lability, temper, disorganization, stress sensitivity, and impulsivity have been shown to respond to treatment with stimulant medications. Non-dopaminergic medications, such as the tricyclic antidepressants and SSRIs

have generally not been useful in adults with ADHD in the absence of depression or dysthymia. Pemoline is no longer approved for use in these patients, despite early favorable reports. Appropriate management of adult patients with ADHD is multimodal. Psychoeducation, counseling, supportive problem-directed therapy, behavioral intervention, coaching, cognitive remediation, and couples and family therapy are useful adjuncts to medication management. Concurrent supportive psychosocial treatment or polypharmacy may be useful in treating the adult with comorbid ADHD.

Effects of diets high in sucrose or aspartame on the behavior and cognitive performance of children.

Wolraich ML, Lindgren SD, Stumbo PJ, Stegink LD, Appelbaum MI, Kiritsy MC. Department of Pediatrics, Vanderbilt University, Nashville, TN.

N Engl J Med. 1994 Feb 3;330(5):301-7

BACKGROUND. Both dietary sucrose and the sweetener aspartame have been reported to produce hyperactivity and other behavioral problems in children.

METHODS. We conducted a double-blind controlled trial with two groups of children: 25 normal preschool children (3 to 5 years of age), and 23 school-age children (6 to 10 years) described by their parents as sensitive to sugar. The children and their families followed a different diet for each of three consecutive three-week periods. One diet was high in sucrose with no artificial sweeteners, another was low in sucrose and contained aspartame as a sweetener, and the third was low in sucrose and contained saccharin (placebo) as a sweetener. All the diets were essentially free of additives, artificial food coloring, and preservatives. The children's behavior and cognitive performance were evaluated weekly.

RESULTS. The preschool children ingested a mean (+/- SD) of 5600 +/- 2100 mg of sucrose per kilogram of body weight per day while on the sucrose diet, 38 +/- 13 mg of aspartame per kilogram per day while on the aspartame diet, and 12 +/- 4.5 mg of saccharin per kilogram per day while on the saccharin diet. The school-age children considered to be sensitive to sugar ingested 4500 +/- 1200 mg of sucrose per kilogram, 32 +/- 8.9 mg of aspartame per kilogram, and 9.9 +/- 3.9 mg of saccharin per kilogram, respectively. For the children described as sugar-sensitive, there were no significant differences among the three diets in any of 39 behavioral and cognitive variables. For the preschool children, only 4 of the 31 measures differed significantly among the three diets, and there was no consistent pattern in the differences that were observed.

CONCLUSIONS. Even when intake exceeds typical dietary levels, neither dietary sucrose nor aspartame affects children's behavior or cognitive function.

Developmental instability and working memory ability in children: a magnetic resonance spectroscopy investigation.

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This study of children (ages 7 through 12) wishes to determine (a) whether variation in frontal lobe brain chemistry, determined from proton magnetic resonance spectroscopy (1H-MRS), is related to performance on a working memory task in children, and (b) whether developmental instability (DI; the imprecise expression of the genetic plan for development due to several known genetic and environmental effects) underlies phenotypic variation in brain chemistry. 1H-MRS assessed neurometabolites in a right frontal white matter voxel. The Visual Two-Back test assessed working memory. A composite measure of DI was created from measures of minor physical anomalies, fluctuating asymmetry of body characteristics, and fluctuating asymmetry of dermatoglyphic features. Greater DI strongly predicted lower concentrations of creatine-phosphocreatine (Cre) and choline-containing compounds, whereas Cre and N-acetyl-aspartate positively correlated with working memory skills. Working memory skills thus seem related to frontal lobe energy metabolism, which in turn is related to DI.

Trends in the prescribing of psychotropic medications to preschoolers.

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CONTEXT: Recent reports on the use of psychotropic medications for preschool-aged children with behavioral and emotional disorders warrant further examination of trends in the type and extent of drug therapy and sociodemographic correlates.

OBJECTIVES: To determine the prevalence of psychotropic medication use in preschool-aged youths and to show utilization trends across a 5-year span.

DESIGN: Ambulatory care prescription records from 2 state Medicaid programs and a salaried group-model health maintenance organization (HMO) were used to perform a population-based analysis of three 1-year cross-sectional data sets (for the years 1991, 1993, and 1995).

SETTING AND PARTICIPANTS: From 1991 to 1995, the number of enrollees aged 2 through 4 years in a Midwestern state Medicaid (MWM) program ranged from 146,369 to 158,060; in a mid-Atlantic state Medicaid (MAM) program, from 34,842 to 54,237; and in an HMO setting in the Northwest, from 19,107 to 19,322.

MAIN OUTCOME MEASURES: Total, age-specific, and gender-specific utilization prevalences per 1000 enrollees for 3 major psychotropic drug classes (stimulants, antidepressants, and neuroleptics) and 2 leading psychotherapeutic medications (methylphenidate and clonidine); rates of increased use of these drugs from 1991 to 1995, compared across the 3 sites.

RESULTS: The 1995 rank order of total prevalence in preschoolers (per 1000) in the MWM program was: stimulants (12.3), 90% of which represents methylphenidate (11.1); antidepressants (3.2); clonidine (2.3); and neuroleptics (0.9). A similar rank order was observed for the MAM program, while the HMO had nearly 3 times more clonidine than antidepressant use (1.9 vs 0.7). Sizable increases in prevalence were noted between 1991 and 1995 across the 3 sites for clonidine, stimulants, and antidepressants, while neuroleptic use increased only slightly. Methylphenidate prevalence in 2- through 4-year-olds increased at each site: MWM, 3-fold; MAM, 1.7-fold; and HMO, 3.1-fold. Decreases occurred in the relative proportions of previously dominant psychotherapeutic agents in the stimulant and antidepressant classes, while increases occurred for newer, less established agents.

CONCLUSIONS: In all 3 data sources, psychotropic medications prescribed for preschoolers increased dramatically between 1991 and 1995. The predominance of medications with off-label (unlabeled) indications calls for prospective community-based, multidimensional outcome studies.