ATTENTION DEFICIT DISORDERS

FRONTAL BRAIN EEG ACTIVATION IN ADHD

Electroencephalographic (EEG) activity of 117 unmedicated children (66 aged 4 years, 51 aged 8 years) with attention deficit/hyperactivity disorder (ADHD) was analyzed at the Department of Child and Adolescent Psychiatry and Psychotherapy, Central Institute of Mental Health, Mannheim, Germany. Boys with ADHD had reduced right frontal brain activity, compared to controls. These differences were specific to the frontal regions, and were not observed in central and occipital EEG patterns. Girls with ADHD had increased right-lateralized frontal activation patterns compared to normal control girls; the asymmetry was opposite to that found in boys with ADHD. Both 4 and 8-year-old children showed these changes. Children with ADHD and comorbid oppositional defiant disorder showed similar EEG changes to those with ADHD alone. This EEG baseline activity reflecting functional changes in the frontal areas correlates with previously reported MRI changes in ADHD. (Baving L, Laught M, Schmidt MH. Atypical frontal brain activation in ADHD: Preschool and elementary school boys and girls. J Am Acad Child Adolesc Psychiatry Nov 1999;38:1363-1371). (Reprints: Dr Baving, Central Institute of Mental Health, Department of Child and Adolescent Psychiatry and Psychotherapy, PO Box 12 21 20, 68072 Mannheim, Germany).

COMMENT. Boys with ADHD have a right frontal lobe deficit, as determined by EEG laterality scores (alpha-1 8-10 Hz), whereas girls with ADHD show the opposite activation pattern, with enhanced left frontal alpha power, corresponding to a left frontal deficit. These changes in frontal brain activation in ADHD may indicate a disorder in the development of regulation of behavior and attention, stemming from a deficit in behavioral inhibition.

Quantitative MRI studies at the National Institutes of Health, Bethesda, MD, and other centers have demonstrated decreased volume of the prefrontal cortex, caudate nucleus, and globus pallidus on the right side of the brain of ADHD boys, pointing to a dysfunction of right-sided prefrontal-striatal systems (see Progress in Pediatric Neurology III, PNB Publ, 1997;pp212-213).

These studies emphasize the neurologic basis for ADHD, as distinct from a purely psychiatric disorder, a concept emphasized by Gordon M in a recent review article (Attention deficit hyperactivity disorder: diagnosis and management in the USA. J R Soc Med Sept 1999;92:453-455). The author correctly emphasizes that the diagnosis and treatment of ADHD should be reserved for patients with evidence of functional impairment. He cautions against the use of the overall IQ as a measure of the expected level of performance and academic achievement in school. Rather, the ADHD diagnosis should be reserved for significant disabilities relative to the general population, a viewpoint that may be questioned by many authorities.

ADHD-RELATED RISK FACTORS FOR EARLY DRUG USE

The risk of early drug use asociated with ADHD was evaluated in a community-based sample of 717 (412 low birth weight, 305 normal birth weight) children examined at 6 years of age and at follow-up at age 11 years, at the Department of Psychiatry, Henry Ford Health Sciences Center, Detroit, MI. Of 137 (19%) who had used drugs at least once, 10.6% had used tobacco, 10.1% alcohol, 3.8% inhalants, and only 7 children had used marijuana. Independent of low or normal birth weight, ADHD at age 6 years increased the odds of drug use to 1.7

compared to 1 in non-ADHD children; the incidence of drug use by 11 years of age was 29% in ADHD compared to 16% in non-ADHD children. The higher the number of ADHD symptoms, the higher the risk of drug use. The higher the incidence of externalizing behavior problems associated with ADHD, the greater the risk of drug use; the odds of drug initiation in children with ADHD versus without ADHD was 2.09 (35% vs 20.1%). Internalizing problems at age 6 showed no association with drug use by age 11. Low levels of parent monitoring and high drug use by peers increased the risk of drug use, independent of the ADHD. Treatment of ADHD with methylphenidate (MPH) was unrelated to the risk of drug use; the incidence of drug use was 31% in those treated and 28% in children not receiving MPH (20% of children with ADHD were on stimulant therapy at 11 years of age). (Chilcoat HD, Breslau N. Pathways from ADHD to early drug use. J Am Acad Child Adolesc Psychiatry Nov 1999;38:1347-1354). (Reprints: Dr Chilcoat, Psychiatry Research, Henry Ford Health Sciences Center, 1 Ford Place, 3A, Detroit, MI 48202).

COMMENT. Children with ADHD at 6 years of age have an increased risk of drug use by age 11 years. Externalizing behavior problems, inadequate parent monitoring, and drug use by peers increase the risk of drug use. Early treatment of behavior and conduct disorders often associated with ADHD, increased parent monitoring, and reduced association with drug-using peers might be effective in reducing the incidence of drug use in children with ADHD.

Effects of stimulant treatment on drug abuse. Stimulant treatment of ADHD neither increases nor decreases the risk of early drug use in the Detroit study, a finding at variance with that of Biederman J, et al (Pediatrics 1999;104:e20), who found that children with ADHD who received stimulants for at least 4 years were at a significantly reduced risk for developing substance abuse disorder than unmedicated children. Contrary to some reports that stimulant medication may encourage later substance abuse in children with ADHD, the report by the Massachusetts General Hospital researchers indicates a protective effect from stimulant therapy.

Drug use in adults with persisting ADHD. Childhood onset ADHD, persisting in adults without psychiatric comorbidity, carried a 52% lifetime risk of drug (mainly marijuana) and drug plus alcohol use compared to 27% of non-ADHD adults. (Biederman J et al, 1995; see Progress in Pediatric Neurology III, PNB Publ, 1997;pp232-233). Psychiatric comorbidy increases the risk of drug abuse in adults.

Psychiatric comorbidity with ADHD. In a study of 105 child and adolescent twins with, and 95 without, ADHD at the University of Colorado, Boulder, CO, inattentive subtypes were associated with lower IQ and higher levels of depression, whereas hyperactivity-impulsivity was associated more strongly with ODD and CD. Combined types were associated with more disruptive behavior than the other 2 subtypes. (Willcutt EG et al. J Am Acad Child Adolesc Psychiatry Nov 199;38:1355-1362).

MPH and Adderal compared in school-age ADHD children. Both stimulants improved teacher and parent behavior ratings. A single dose of Adderal was as effective as two daily doses of MPH. Sadness was the most frequent side effect common to both drugs, occurring in 10-12% at optimal dose levels. (Manos MJ, Short EJ, Findling RL. J Am Acad Child Adolesc Psychiatry July 1999;38:813-819). Adderal may be preferred to MPH in older children, who often object to school involvement in lunch time doses. (see Ped Neur Briefs June

1999;13:44, for previous comparison study of Ritalin and Adderal in ADHD).

HEADACHE DISORDERS

MIGRAINE PATHOPHYSIOLOGY AND TREATMENT

The proceedings of a symposium on "The scientific basis of migraine management" held Feb 1999 at Lake Louise, Alberta, Canada, are reported from the University of Calgary and other centers. (Becker WJ, et al. Can J Neurol Sci Nov 1999;26: Suppl 3).

Pathophysiology. Local vasodilatation of intracranial extracerebral blood vessels, and consequent stimulation of surrounding trigeminal sensory nervous pain pathways, causes release of vasoactive neuropeptides that sensitize neurons in the brain stem trigeminal nuclei and increase the pain response. The clinical effectiveness of 5-HT serotonergic agonists (triptan anti-migraine agents) is related to vasoconstriction, and inhibition of nociceptive transmission in peripheral nerve terminals in the meninges and in central terminals in brain stem sensory nuclei. (Hargreaves RJ, Shepheard SL. Pathophysiology of migraine - new insights. Can J Neurol Sci 1999;26:Suppl 3-S12-S19).

Biology of Serotonin Receptors. Serotonin receptors are highly heterogeneous (5-HT,1-7), and specific subtypes are associated with the pathogenesis or treatment of migraine headache. Availability of subtype selective 5-HT receptor agonists allow further proof of the neural/vascular hypothesis for migraine. (Hamel E. Can J Neurol Sci 1999;26:Suppl 3-S2-S6).

Genetic basis of migraine. Migraine etiology is multifactorial and genetically complex, with aggregation in families due to environmental and genetic tendencies. Familial hemiplegic migraine (FHM) is autosomal dominant, with 50% of families linked to chromosome 19p13 and mutations in a calcium channel alpha 1A subunit. FHM represents a CNS channelopathy. Migraine with or without aura may also be linked to chromosome 19p, or to Xq28 locus. (Gardner K. Can J Neurol Sci 1999;26:Suppl 3-S37-S43).

Migraine prophylactic drug therapy. The scientific evidence based on randomized double-blind, placebo controlled trials, rates migraine prophylactics in the following order of efficacy: metoprolol has an average score of 4.3 (maximum 5); divalproex 3.8; amitriptyline 2.3; atenolol 2.3; flunarazine 2.2; and propranolol 1.4. The placebo response varies from a 32% reduction in migraine frequency to a 7% increase in frequency in various trials. Migraine prophylaxis is largely disappointing, a minority having significant benefits that make the risk of adverse effects worthwhile. Other newer antimigraine agents include the antiepileptics, gabapentin and topiramate, and riboflavin. A combination of an antidepressant and a B-blocker may act synergistically, but monotherapy is often preferred. (Becker WJ. Evidence based migraine prophylactic drug therapy. Can J Neurol Sci 1999;26:Suppl 3-S27-S32).

COMMENT. This journal supplement provides an excellent review of the scientific advances in migraine mechanism and management. One paper also emphasizes the role of psychological treatments, especially relaxation training and biofeedback, in refractory migraine. The following report might also indicate the influence of psychological factors on the frequency of migraine attacks.