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ATTENTION DEFICIT AND LEARNING DISORDERS

GENETIC INFLUENCES IN ADHD

The genetic influences in pediatric behavior and attention disorders, attention deficit hyperactivity disorder and autism, are reviewed from the Department of Psychiatry, UCLA School of Medicine, Los Angeles, CA. ADHD is a familial disorder, with frequency 5 to 6-fold greater among first-degree relatives than in the general population. An autosomal gene may be involved. In twin studies using interview assessment of ADHD, concordance of 79% was found in 37 monozygotic twins compared to 32% in 37 same-sex dizygotic twins. Relatives of ADHD probands have increased rates of comorbid conditions, especially oppositional and conduct disorders, anxiety, mood disorders, and learning disabilities. Family studies suggest that comorbid disorders can be independently transmitted or may reflect specific subtypes of ADHD. Shared environmental factors may contribute to the comorbidity. Adoption studies support both a genetic basis for ADHD and environmental factors. The possible genetic influence in the association of ADHD and tic disorders is not resolved. Ongoing investigations of ADHD etiologies involve candidate-gene studies of dopamine-related genes, and prenatal environmental factors affecting the developing brain. (Smalley SL. Behavioral genetics '97. Genetic influences in childhood-onset psychiatric disorders: autism and attention deficit/hyperactivity disorder. Am J Hum Genet June 1997;60:1276-1282). (Reprints: Dr Susan L Smalley, Department of Psychiatry, 47-438 NPI, UCLA School of Medicine, 760 Westwood Plaza, Los Angeles, CA 90024).

COMMENT. Both genetic and environmental factors affecting brain development appear to be important in the pathophysiology of ADHD.

ADHD AND FRONTAL-MOTOR CORTEX DISCONNECTION

The neurological concept involving the frontal lobe in the mechanism of attention deficit hyperactivity disorder is reemphasized by neurologists and geneticists at the Johns Hopkins University School of Medicine, Baltimore, MD. A frontal-motor cortex disconnection syndrome, or "lazy" frontal lobe, in

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ADHD is hypothesized on the basis of cerebral blood flow and EEG studies, and MRI findings. The concept develops from the function of the frontal lobe as an inhibitor of excessive motor activity, and children with ADHD having disinhibited motor activity. The calming effect of methylphenidate stems from its stimulatory effect on the frontal lobe causing motor inhibition. (Niedermeyer E, Naidu SB. Attention-deficit hyperactivity disorder (ADHD) and frontal-motor cortex disconnection. Clin Electroencephalogr July 1997;28:130-136). (Reprints: Ernst Niedermeyer MD, Johns Hopkins Hospital, Room 2-147, Meyer Building, 600 N Wolfe Street, Baltimore, MD 21287).

COMMENT. The importance of the frontal lobe in relation to hyperactive behavior was demonstrated more than 50 years ago in animal studies by Langworthy and Richter (1939), and later by Livingston, Fulton and colleagues (1948), and Mettler (1967). Two types of hyperactivity were distinguished: *overreactivity*, an external stimulation or distractibility caused by frontal lobe injury, and *essential overactivity*, a disinhibitive hyperkinesia due to striatal lesions and release from fronto-cortical-reticular inhibition of ascending systems. (See Progress in Pediatric Neurology III, Ed. Millichap JG, PNB Publ, pp195-265, for further articles and comments on the neurobiologic organic theory of ADHD). Since the report of 3 children with a temporal lobe arachnoid cyst TLAC/ADHD syndrome (Millichap JG. Neurology May 1997;48:1435-1439), three further cases have been uncovered. Different sites and degrees of damage in the cortical striatal circuit might account for the heterogeneous nature of ADHD.

HIPPOCAMPAL SCLEROSIS AND COGNITIVE DYSFUNCTION

Deficits of cognitive function, including language development and learning of complex social skills, typical of mental deficiency and autism, are reported in 4 children with bilateral hippocampal sclerosis and epilepsy followed at Duke University Medical Center, Durham, NC. MRI showed increased signal on T2-weighted images and 25% loss of volume of the hippocampi, pictures consistent with sclerosis. An early normal development was interrupted by episodes of status epilepticus, followed by failure of language development and social deficits. Control of seizures was not accompanied by improved social/adaptive skills. The hippocampus is essential for learning of language and social development in infancy. (DeLong GR, Heinz ER. The clinical syndrome of early-life bilateral hippocampal sclerosis. Ann Neurol July 1997;42:11-17). (Respond: Dr DeLong, Division of Pediatric Neurology, Box 3936, Duke University Medical Center, Durham, NC 27710).

COMMENT. Bilateral hippocampal sclerosis in infancy may result in failure of language development and deficits in behavior and social learning consistent with mental retardation and autism. Normal acquisition of language and learning is not significantly affected by unilateral damage to the hippocampus. Neuronal loss in the hippocampi during prolonged seizures has been linked to excessive release of glutamate.

RIGHT BRAIN DOMINANCE IN INFANCY

The functional development of the left and right cerebral hemispheres in 39 normal children, aged 18 days to 19 years, was studied by measurements of cerebral blood flow at rest, using single photon emission computed tomography (SPECT), at the Neuropediatric Department, Hospital Saint Vincent de Paul, Paris, France. Functional brain activity and blood flow were greater in