

COMMENT. Infantile bilateral striatal necrosis is characterized by degeneration of the caudate nucleus, putamen, and occasionally the globus pallidus. Clinically, the disease presents with developmental regression, choreoathetosis, dystonia, spasticity, failure to thrive, nystagmus, optic atrophy, and mental retardation. Familial cases are described. In the above families, the gene mutation is mapped to chromosome 19q13.33.

ATTENTION DEFICIT DISORDERS

EFFECTS OF METHYLPHENIDATE AND ATOMOXETINE ON CORTICAL INHIBITION IN ADHD

The effects of methylphenidate (MPH), a psychostimulant, and atomoxetine (ATX), a selective norepinephrine reuptake inhibitor, on short interval-cortical inhibition (SICI) were measured in motor cortex with transcranial magnetic stimulation, in a study at Cincinnati Children's Medical Center, OH, and other centers. The study was randomized, double-blind, single-dose, and crossover, comparing 0.5 mg/kg MPH with 1.0 mg/kg ATX in 16 children with ADHD, aged 8-17 years. Seven were homozygotes and 9 heterozygotes for the dopamine transporter, DAT1, a site of action of MPH. MPH and ATX had similar effects on SICI, but their effects differed significantly by DAT1 genotype ($P=0.0008$). MPH and ATX increased SICI in heterozygotes but not in 10-repeat homozygotes. A genetic variation in DAT1, a known link to risk of ADHD, can influence the neurophysiological effects of MPH and ATX. (Gilbert DL, Wang Z, Sallee FR et al. Dopamine transporter genotype influences the physiological response to medication in ADHD. *Brain* August 2006;129:2038-2046). (Respond: Donald L Gilbert MD MS, Cincinnati Children's Hospital Medical Center, Division of Neurology, ML #2015, 3333 Burnet Ave, Cincinnati, OH 45229).

COMMENT. Motor cortical inhibition is impaired in ADHD and correlates with symptom severity and medication response. Whereas MPH and ATX have similar effects on short interval cortical inhibition (SICI), the effects vary with the dopamine transporter (DAT1) genotype. Both drugs increase SICI toward normal in heterozygotes but not in homozygotes. These results are in agreement with reports of a poor clinical response to MPH in ADHD patients with the DAT1 10/10 homozygous genotype.

Long-term effects of atomoxetine in 6-7 year-old children with ADHD. In a meta-analysis of 7 double-blind/placebo-controlled and 6 open-label studies, effectiveness of ATX was maintained in 70% of 97 subjects treated for >2 years; 25.7% discontinued therapy because of lack of effectiveness and 4% because of adverse events. The mean actual height at 24 months was 2.7 cm less than that expected; mean height percentile was 54.3 at baseline, 42.9 at 18 months, and 43.4 at 24 months. The mean actual weight at 24 months was 2.5kg lower than expected; weight percentile was 62.6 at baseline, 50.3 at 18 months, and 51.0 at 24 months. Cardiovascular effects included significant increases in pulse (mean change 7.2 bpm; $P<0.001$), diastolic BP (mean increase 3.4 mmHg; $P<0.001$), and systolic BP (mean increase 3.7 mmHg; $P<0.001$). Increases in BP over time were considered to be age related. ECG-corrected QT interval increase of 0.2 msec was not significant, but PR interval was significantly shortened (mean change -4.3 sec; $P<0.001$). (Kratochvil CJ, et al. *J Am Acad Child Adolesc Psychiatry* August 2006;45:919-927).