### MOVEMENT DISORDERS

## NEURAL BASIS OF TICS: A FUNCTIONAL MRI STUDY

Event-related functional MRI (fMRI) was used to study the neural basis of spontaneous motor and vocal tics in 10 patients with Tourette syndrome, at the National Institute of Neurological Disorders and Stroke, Bethesda, MD. MRI activities were analyzed 2 seconds before and at tic onset, by synchronized video/audio recordings. Before the onset of tics, activated paralimbic areas included anterior cingulate and insular cortex, supplementary motor area and parietal operculum. At tic onset, fMRI activity occurred in sensorimotor areas including suprior parietal lobules and cerebellum. The paralimbic and sensory association areas involved in tic generation are similar to those implicated in movements triggered internally by unpleasant or emotional sensations, such as pain and itching. (Bohlhalter S, Goldfine A, Matteson S et al. Neural correlates of tic generation in Tourette syndrome: an event-related functional MRI study. **Brain** August 2006;129:2029-2037). (Respond: Mark Hallett, Human Motor Control Section, National Institute of Neurological Disorders and Stroke (NINDS), NIH, Building 10, Room 5N226, 10 Center Drive, MSC-1430, Bethesda, MD 20892).

COMMENT. The authors postulate a limbic overdrive of the motor system and activation of sensorimotor areas underlying the pathophysiology of tic generation. The unpleasant urge and psychic tension that precede and trigger tics are similar to those of pain or itching, and involve the same paralimbic and sensory areas demonstrated by fMRI for tics. The distinction between the neural basis of involuntary motor tics and tics voluntarily acted out to bring momentary relief of the unpleasant sensation needs further study.

#### **GENETICS OF INFANTILE BILATERAL STRIATAL NECROSIS**

The gene mutation causing autosomal recessive infantile bilateral striatal necrosis (IBSN) was identified in eight consanguineous Israeli Bedouin families, in a study at Schneider Children's Medical Center, Petah Tikva, Israel, and other centers. The age of onset of the disease in the 12 affected individuals ranged from 7 to 15 months. Choreoathetoid movements of the face, trunk and extremities, dystonia, pendular nystagmus, optic atrophy, and spastic quadriparesis were associated with gradual disappearance of the basal ganglia on serial MRI scans. At 10 to 11 years old, the MRI showed a small, residual caudate nucleus and putamen with abnormal signals. Metabolic workup was normal. Sequencing of the nup62 gene showed a missense mutation in all patients mapped to the chromosomal region 19q13.33. Five prenatal diagnoses were made in 3 at-risk families. The p62 protein is involved in the basal ganglia degeneration. (Basel-Vanagaite L, Muncher L, Straussberg R et al. Mutated nup62 causes autosomal recessive infantile bilateral striatal necrosis. Ann Neurol August 2006;60:214-222). (Respond: Dr Basel-Vanagaite, Department of Medical Genetics, Schneider Children's Medical Center of Israel and Rabin Medical Center, Beilinson Campus, Petah Tikva, 49100 Israel).

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 metaanalysis 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).