MUSCLE DISORDERS

LIMB-GIRDLE MUSCULAR DYSTROPHY

Sixty-one members of a large Spanish kindred with autosomal dominant limb-girdle muscular dystrophy (LGMD), spanning 5 generations, were examined at the Hospital Vail d'Hebron, Barcelona and other centers. Characteristic proximal muscle weakness involving pelvic and shoulder girdle muscles was found in 32 patients (15 men, 17 women) between the ages of 7 and 66 years (mean 34 years). Age at onset ranged from less than 1 to 58 years (mean 16 years). A *juvenile* form (onset before 15 years) and an *adult-onset* form (30-40 year onset) were identified in 72 and 28%, respectively. Weakness extended to distal muscles late in the course in adult cases, but generalized weakness occurred at initial presentation in severely affected juvenile cases. Progression was slow in adult cases and relatively faster in juvenile-onset cases. Severity worsened in successive generations (anticipation) among 26 parent-child pairs. None had ptosis, ophthalmoplegia, dysphagia, speech disorders, calf hypertrophy, myalgia, or mental deterioration. Muscle biopsy on 5 patients showed nonspecific findings compatible with MD; rimmed vacuoles were present in 3. Linkage analysis findings were distinct from previously reported forms of LGMD (1A - E), and chromosomes 5q31, 1q11, 3p25, 6q23, and 7q linkages were identified. (Gamez J, Navarro C, Andreu AL et al. Autosomal dominant limb-girdle muscular dystrophy. A large kindred with evidence for anticipation. Neurology February (2 of 2) 2001;56:450-454). (Reprints: Dr Josep Gamez, Department of Neurology, Hospital Gral, Vail d'Hebron, Passeig Vail d'Hebron, 119-125, 08035 Barcelona, Spain).

COMMENT. A genetically distinct form of autosomal dominant limb-girdle muscular dystrophy (LGMD) is added to the previously described 5 types of AD-LGMD (1 A-E). Characteristic features of LGMD include: slowly progressive proximal symmetric weakness with predominantly pelvic onset, normal to mildly elevated CK, myopathic EMG and muscle biopsy, and negative immuno-histochemical stains for dystrophin and sarcoglycans. Extraocular, facial, and bulbar muscles are unaffected. Two clinical types are identified (juvenile and adult-onset), according to age at onset, severity of muscle involvement, and rate of progression. In almost two-thirds, onset is in childhood or adolescence. Earlier onset in children than in parents suggests genetic anticipation, but disease severity is unrelated to the parent's gender.

ATTENTION DEFICIT DISORDERS

COMORBID ADHD AND TIC DISORDER

Motor system excitability was measured in 16 children with ADHD, 16 with chronic tic disorder or Tourette's disorder (TD), 16 with comorbid ADHD and TD, and 16 healthy control children, in a study at the University of Gottingen, Germany. The technique of focal transcranial magnetic stimulation (TMS) was used in a single and paired-stimulus paradigm, to assess inhibitory mechanisms within the motor system of these 4 groups. Children with ADHD alone had a reduced intracortical inhibition compared to those without ADHD, confirming deficits in inhibitory cortical motor mechanisms in ADHD. Children with TD had a shorter cortical silent period on TMS than those without TD, correlating with a deficient motor inhibition in the sensorimotor circuit. Children with combined ADHD and TD had both a significantly reduced intracortical inhibition and a shortened cortical silent period, suggesting an additive deficit in motor system

inhibition at the level of motor system excitability. (Moll GH, Heinrich H, Trott G-E, Wirth S, Bock N, Rothenberger A. Children with comorbid attention-deficit-hyperactivity disorder and tic disorder: Evidence for additive inhibitory deficits within the motor system. Ann Neurol March 2001;49:393-396). (Respond: Prof Rothenberger, von-Siebold-Str 5, D-37075 Gottingen, Germany).

COMMENT. Children with comorbid ADHD and TD have additive deficits in motor system inhibition, involving both cortical motor mechanisms and the sensorimotor circuit. This finding is thought to be in line with neuropsychological data suggesting most severe impairments of motor inhibition in ADHD combined with TD.

Motivational effects on inhibitory control in children with ADHD.

Lowered inhibitory control in children with ADHD is attributed to low motivational incentive in a study of 33 children using a stop-signal task, at the University of Essen, Germany. (Slusarek M et al. J Am Acad Child Adolesc Psychiatry March 2001;40:355-363). Under conditions of low incentives, children with ADHD were less able to inhibit reactions and had longer stop-signal reaction times. With high incentives, they performed as well as controls. From a practical standpoint, the implementation of motivational incentives in ADHD individuals is often a problem, however.

COMORBID ADHD/DEPRESSION TREATED WITH BUPROPION SR

A trial of bupropion sustained release (SR) was conducted in 24 adolescents (ages 11-16 years) with ADHD and either major depressive disorder or dysthymic disorder at the Department of Psychiatry, Dartmouth Medical School, Hanover, NH. The mean final titrated doses were 2.2 mg/kg qam and 1.7 mg/kg qpm, with a maximum of 3 mg/kg bid. Outcomes were rated by the clinician, parent, child, and teachers. Fourteen (58%) showed a global improvement in both ADHD and depression on clinician ratings; the response was in depression only in 29%. and in ADHD only in 4%. Parents' and childrens' ratings of depression after bupropion improved significantly, when compared to prior placebo ratings. Parents' ratings of ADHD improved while teachers' ratings did not. Final parents' ratings of functional impairment showed significant improvements. All subjects completed the 2-week single-blind placebo lead-in and the 8 week bupropion trial. Comparing bupropion versus placebo periods, rash occurred in 13% vs 8%; irritability in 8% vs 4%;. tremor in 4% vs 0%; and motor tics in 4% vs 0%. No patient discontinued medication compietely because of side effects. (Daviss WB, Bentivoglio P, Racusin R et al. Bupropion sustained release in adolescents with comorbid antention-deficit/hyperactivity disorder and depression. J Am Acad Child Adolesc Psychiatry March 2001;40:307-314). (Respond: Dr Daviss, Western Psychiatric Institute and Clinic, 3811 O'Hara St, Pittsburgh, PA 15213).

COMMENT. Bupropion SR may be effective in adolescents with depression and ADHD and further controlled studies are indicated. The teachers' failure to observe improvement in ADHD symptomatology is disappointing, and the occurrence of rash, irritability, tremor, and tics is noteworthy. The lack of seizures as a side effect in this study is encouraging, though the drug should be avoided or used with caution in patients with a predisposition to seizures.