

Developmental stuttering is associated with atypical planum temporale asymmetry, in a study by Foundas AL et al, 2001, and cited in an editorial (Foundas AL. Brain lumps and bumps: a neural risk for autism *Ann Neurol* Dec 2004;56:755-756). Cortical structures implicated in language deficits are not smaller but larger, and “bigger is not always better.” Foundas proposes that the alterations in cellular morphology may affect a single cortical layer or may be more extensive and associated with minor heterotopias. The relation between brain morphology, language, and genetics is a potentially important area of research in autism and SLI.

Discordant mental and physical efforts in autism. Ming X, et al (*Brain Dev* Dec 2004;26:519-524) monitor brainstem autonomic function to detect mental effort in a child with autism and non-compliance. The patient showed decreases in cardiac vagal tone and cardiac sensitivity to baroreflex, and sustained increases of mean arterial blood pressure and heart rate concurrently, indicating an appropriate autonomic response to a mental effort but failed physical effort. The discordant mental and physical efforts indicate that the autistic patient does comply with commands mentally, and attempts to modify behavior through medications or behavioral intervention may be ill-advised.

Children’s Communication Checklist to differentiate autism and ADHD. Compared to normal controls, children with High Functioning Autism showed language deficits on all CCC scales, and the information obtained on the CCC was different for ADHD and autism patients. Information obtained from both parent and teacher increased patient identification compared to that of parent alone. (Geurts HM, et al. Can the Children’s Communication Checklist differentiate between children with autism, children with ADHD, and normal controls? *J Child Psychology and Psychiatry* Nov 2004;45:1437-1453).

MOVEMENT DISORDERS

CLINICAL FEATURES OF RESTLESS LEGS SYNDROME

Clinical characteristics of childhood-onset restless legs syndrome (RLS) were studied in 32 (5.9%) patients, <18 years of age, diagnosed with the disorder among 538 who attended the Pediatric Sleep Disorders Center with sleep-wake complaints, between January 2000 and March 2004, at the Mayo Clinic, Rochester, MN. Subjects with RLS were classified as *probable* (9/32 [28%]) or *definite* (23/32 [72%]). The age of diagnosis was earlier in the probable group (11.3 years; range 6-15) than the definite group (13.9 years; range 5-17; $p=0.04$), but otherwise, no differences were found between the two groups. All patients met the diagnostic criteria for RLS as defined by the National Institutes of Health workshop (Allen RP, et al. *Sleep Med* 2003;4:101-119). These include an urge to move the legs, accompanied by unpleasant sensation in the legs, worsened by periods of inactivity, relieved by movement, occurring mainly at night, complicated by sleep disturbance, and a positive family history. The average duration of follow-up was 12.3 months (range 1-44). Sleep onset or sleep maintenance insomnia was the most common complaint occurring in 28 of 32 (87.5%) patients, inattentiveness was present in 25%, limb movements observed during sleep as a presenting symptom in 31%, chronic fatigue in 28%, and sleep walking in 9.3%. A

positive family history of RLS in first-degree relatives was obtained in 23 of 32 subjects (71%); mothers were affected more often than fathers (17/23 cf 6/23; $p=0.02$). Serum ferritin levels, available in 24 of 32 subjects, were below the 5th percentile for age and sex in 8 (33%) (5th percentile norms in 10-year-old boys are 24mcg/L and in adolescent girls 8mcg/L); and below the median (23 mcg/L in males and 17 mcg/L in females) in 18 (75%); 20 (83%) subjects had levels below 50 mcg/L (normal median values range from 29 to 52mcg/L). Hematocrit was below the reference range in 5 of 23 subjects (mean 33.9; range 32.8-35). The mean Periodic Limb Movement Index (PLMI) in 24 subjects was 17.3 and greater than 5 in 16 (67%). Sleep was improved by pharmacotherapy in 18 of 29 (62%) subjects (pramipexole [dopamine receptor agonist], oral iron, gabapentin, clonazepam, or carbidopa-L-dopa) and unchanged in 4 (14%); in 7 the response was unknown. (Kotagal S, Silber MH. Childhood-onset restless legs syndrome. *Ann Neurol* December 2004;56:803-807). (Respond: Dr Kotagal, Division of Child Neurology, Mayo Clinic, 200 First Street SW, Rochester, MN 55905).

COMMENT. Restless legs syndrome (RLS) occurs in two forms, primary and secondary. The primary form has an early age of onset and is inherited as a single, autosomal dominant genetic disorder with a predilection for maternal transmission. In the above study, mothers were affected three times more often than fathers. The secondary form occurs in association with iron deficiency, anemia, pregnancy, renal failure, Charcot-Marie Tooth type 2 disease, spinocerebellar ataxia, and Parkinson disease (Rye DB. *Neurology* December (2 of 2) 2004;63:2213-2214). A decrease in serum ferritin levels is a significant feature of RLS, previously described in teenagers (Kryger MH et al. *Sleep Med* 2002;3:127-132) and adults (Sun ER et al. *Sleep* 1998;21:371-377) with RLS. Oral iron therapy may result in improved sleep-wake function and relief of RLS (Kryger et al, 2002; Allen RP. *Sleep Med* 2004;5:385-391). Decreased serum ferritin levels are not always associated with low hematocrit or low red cell mean corpuscular volume; anemia is a late finding, when the serum ferritin has fallen below 10 mcg/L (Halberg L, Hulthen L. *Blood Cells Mol Dis* 2002;29:562-573). Adolescent girls may be at greater risk of exacerbation of RLS because of lower iron stores during menstruation. Serum ferritin measurements are an important diagnostic aid in childhood-onset RLS, and oral iron therapy may be of benefit in therapy.

RLS may occur in association with attention deficit hyperactivity disorder (ADHD) (Picchietti DL et al. *Mov Disord* 1999;14:1000-1007), and both daytime and nighttime behavioral symptoms need to be addressed in the workup of RLS. Inattention was noted as a feature in 25% of RLS cases reported from the Mayo Clinic. Periodic limb movements in sleep (PLMs) are another comorbid disorder, occurring in association with childhood RLS, ADHD and sleep disorders (Picchietti et al, 1999). PLMs consist of extension of the big toe, similar to a Babinshi sign, flexion of the foot, and an abrupt extension of the limb. These repetitive, stereotyped movements, associated with sleep disorders, on arousal or awakening, are frequently overlooked by parents and physicians, they are diagnosed by polysomnography, and they can occur independently of RLS (Martinez S, Guilleminault C. *Dev Med Child Neurol* November 2004;46:765-770). Both RLS and PLM respond to treatment with the dopamine agonist pramipexole.

Cabergoline treatment in RLS. The dopamine agonist cabergoline (CAB) was effective in the treatment of 85 adults (71% females) with RLS in a double-blind, placebo-controlled, multicenter trial followed by an open long-term extension trial of 47 weeks

(Stiasny-Kolster K et al. **Neurology** December (2 of 2) 2004;63:2272-2279). Augmentation or worsening of symptoms, unique to dopaminergics, occurs less often with cabergoline than with shorter acting drugs (9% cf 30% with pramipexole). Cabergoline has a half-life of up to 65 hours, and is currently approved for treatment of adults with Parkinsonism. Pramipexole is currently considered the first line of treatment for idiopathic RLS (Silber M et al. **Mayo Clinic Proc** 2004;79:916-922).

CLINICAL FEATURES OF IDIOPATHIC PAROXYSMAL KINESIGENIC DYSKINESIA

The clinical features of 121 patients, referred for genetic study, with a presumptive diagnosis of idiopathic paroxysmal kinesigenic dyskinesia (PKD), were reviewed by a multicenter panel and reported from the University of California, San Francisco. Patients were interviewed by a single neurologist. Based on the distinctive homogeneous phenotype elicited in 79% of affected subjects, the authors propose the following diagnostic criteria for idiopathic PKD: attacks, mainly dystonic, triggered by sudden movements (100%); precipitated by anxiety or stress (62%), or caffeine (13%); a premonitory sensation (82%); short duration of attacks (<1 minute; <30 sec in 93%); no loss of consciousness; painless; response to antiepileptic drugs (carbamazepine or phenytoin); no recognized alternative organic disease and normal neurologic exam; and age at onset between 1 and 20 years. Cases were familial or sporadic. Familial kindreds had a more variable age at onset, and a frequent history of infantile convulsions. The infantile-onset group of PKD cases (n=12) had less uniform characteristics: a kinesigenic trigger was often absent, attacks sometimes occurred during sleep, and the response to AED (carbamazepine) was not universal. Sporadic cases were more often male, the attack frequency was higher, and males had a lower remission rate than females. Women had a better prognosis and a higher rate of complete remission; many obtained remission during pregnancy. (Bruno MK, Hallett M, Gwinn-Hardy K, et al. Clinical evaluation of idiopathic paroxysmal kinesigenic dyskinesia. New diagnostic criteria. **Neurology** December (2 of 2) 2004;63:2280-2287). (Reprints: Dr LJ Ptacek, Howard Hughes Medical Institute, Department of Neurology, University of California, San Francisco, 1550 4th St, Mission Bay 19B, Rm 546, San Francisco, CA 94143).

COMMENT. This large clinical study of both familial and sporadic cases of PKD provides diagnostic criteria for idiopathic PKD. The age at onset is crucial (<20 years), except in familial cases, and secondary causes such as multiple sclerosis, and vascular, metabolic, or traumatic disorders need to be excluded in patients presenting after 20 years of age. The presence of familial cases is not essential, but a family history of PKD makes the diagnosis more certain. A small group of infantile-onset cases do not conform to strict diagnostic criteria of PKD, and alternative diagnoses include paroxysmal nonkinesigenic dyskinesia (PNKD), occurring without a trigger, shuddering attacks, and benign myoclonus of early infancy. Gene discovery in the future should help to clarify the diagnosis in doubtful cases.

Dystonia in a boy with secondary progressive multiple sclerosis is reported from Kyoto, Japan. (Shiraishi K et al. **Brain Dev** Dec 2004;26:539-541). Presenting at 8 years of age, the dystonia and MS were at first relapsing-remitting, and at 13 years, became progressive.