Skin biopsies, abnormal splicing, and CMT1B

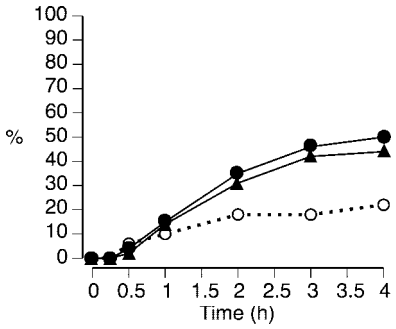
Sabet et al. demonstrate that an intronic mutation in the *MPZ* gene can cause CMT1B by disrupting mRNA splicing. The authors employed dermal skin biopsy to characterize molecular mechanisms of demyelination.

see page 1141

The editorial by Timmerman and Herrmann notes that there is increasing evidence that many disease-causing genes harbor mutations that affect splicing. Such is the case for the MPZ protein involved in CMT neuropathies. To date, more than 100 distinct mutations have been identified in the MPZ gene. Most are missense mutations but four pathogenic intronic MPZ mutations have been reported, including this report. Diagnostic laboratories often sequence only the coding regions of the MPZ gene, but must also screen non-coding intronic sequences. The MPZ gene, encoded by six exons, is expressed by Schwann cells and comprises a major portion of peripheral myelin protein. A trans-membrane protein of 219 amino acids, it belongs to the immunoglobulin gene superfamily. MPZ is a homophilic adhesion molecule, and packs myelin membranes together as a molecular Velcro. The Sabet et al. study supports the utility of skin biopsy in the evaluation of CMT neuropathies, by demonstrating that it can provide information on the molecular mechanism of a pathogenic mutation. Moreover, serial molecular and morphologic analysis of cutaneous nerve bundles of patients with CMT holds promise as a tool to measure effects of new treatments.

see page 1114

Rizatriptan is effective in pediatric migraine

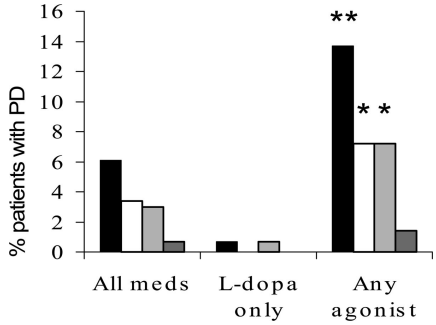


Headache relief (pain-free response). Placebo (○) and the first (●) and second (▲) attack treated with rizatriptan.

Ahonen et al. studied the efficacy of rizatriptan in 116 patients with migraine aged 6 to 17 years in a placebo-controlled three-way crossover trial. Rizatriptan was superior to placebo from 1 hour post-dose, and this response remained similar in the consecutive attack treated with rizatriptan.

see page 1135

Pathologic gambling, hypersexuality, other compulsive behaviors: Occurrence in PD with/without dopamine agonists



Patients with PD (%) with pathologic gambling, hypersexuality, compulsive shopping, or any compulsive behavior.

Voon et al. screened 297 patients with PD for pathologic gambling, hypersexuality, and compulsive shopping. The behaviors were associated with dopamine agonists (13.7%) and not levodopa (0.7%).

see page 1254

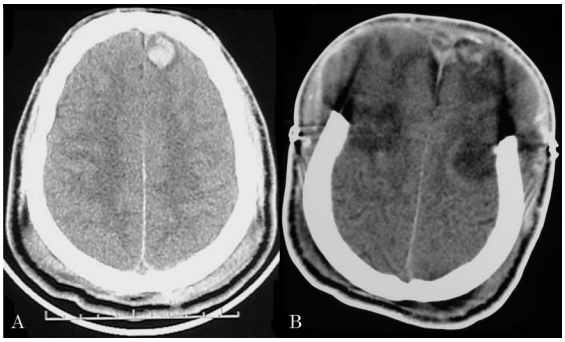
Pontone et al. report that impulse control disease in patients with PD was associated with use of dopamine agonists as well as with depressed mood, disinhibition, irritability, and appetite disturbance.

see page 1258

The editorial by Black and Friedman about these two articles notes that repetitive behavior disorders (termed punding by Joe Friedman) with the drug treatment of PD have been recognized since 1994: peculiar stereotyped behavior characterized by an intense fascination with a repetitive activity. Although hypersexuality was identified in the early days of L-dopa, it was not considered in its current context until other behaviors, particularly gambling, shopping, and eating, were also noted to develop in the setting of dopaminergic medication, particularly the dopamine agonists. The patients reported in these two articles typically were not gamblers, sex- or shop-aholics before they started their PD medications. They were not impulsive by nature. While all antiparkinsonian drugs produce similar psychotic symptoms, the development of a repetitive disorder is rare with L-dopa alone except at high doses but relatively common with the dopamine agonists: 9% and 13.7%. In both articles the D3 receptor-preferring agonist pramipexole was most associated with serious impulsivity. These observations provide a dramatic illustration that problem behaviors, once linked to moral turpitude, may be biochemical in origin and not the result of poor upbringing or deficiencies of moral fiber.

see page 1118

Cerebral infarction and head trauma



Territorial infarction. (A) Admission CT scan: left frontal contusion. (B) CT scan, day 8, 12 hours after decompressive craniectomy: Brain herniation through skull defect, bilateral hypodensity involving frontal cortex and subcortical white matter in the territory of distal MCA branches, sparing the internal frontal gyri.

Marino et al. evaluated 89 patients with moderate or severe head trauma. They found that 17 patients (19.1%) developed cerebral infarctions on brain CT. Cerebral infarction was strongly associated with intracranial hypertension. Patients with cerebral infarction had a worse outcome than patients without infarction.

see page 1165

Albuminuria and stroke hemorrhagic transformation

Rodríguez-Yáñez et al. studied 200 patients with ischemic stroke and found that albuminuria (as a marker of endothelial dysfunction) in the first urine sample was an independent predictor of hemorrhagic transformation.

see page 1172

Cerebellar infarction presenting with isolated vertigo

Lee et al. found that 24 (16.3%) of 147 patients with pure PICA territory cerebellar infarction had isolated prolonged vertigo. Normal head thrust and caloric test results differentiated pseudo-vestibular neuritis associated with mPICA territory cerebellar infarction from true vestibular neuritis.

see page 1178

Gabapentin and postoperative delirium

Leung et al. found that postoperative delirium occurred in 5 out of 12 patients who received placebo vs 0 out of 9 patients who received gabapentin as an add-on agent for postoperative pain. The reduction in delirium may be secondary to the opioid-sparing effect of gabapentin.

see page 1251

The editorial by John Markman notes that the decrease in opioid consumption in patients receiving gabapentin likely accounts for the absence of delirium in this group. Opioid sparing is not an important objective in itself, but reduction in opioid side effects is. In contrast to other factors that predispose to postoperative delirium, adequacy of pain control and choice of analgesics are easily modified. The result of this small study provides proof of concept for the opioid-sparing benefit of gabapentin, and justifies a large, multicenter phase III trial of gabapentin to reduce the rate of postoperative delirium. The antihyperalgesic benefit of gabapentin may be mediated by binding to the α_2-δ subunit Type 1 of the voltage-gated calcium channel.

see page 1116

RESIDENT AND FELLOW SECTION

Call for Teaching Videos

The *Neurology* Resident section is featured online at www.neurology.org. The Editorial Team of this section is seeking teaching videos that will illustrate classic or uncommon findings on movement disorders. Such videos will aid in the recognition of such disorders. Instructions for formatting videos can be found in the Information for Authors at www.neurology.org.

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