Copy number aberrations in hereditary spastic paraplegia

Beetz et al. investigated SPAST gene copy number aberrations in 65 mutation-negative patients with autosomal dominant hereditary spastic paraplegia (AD HSP). Deletions were observed in 12 cases (18%), increasing substantially the number of identified SPAST mutations that combine to account for approximately half of AD HSP cases.

see page 1926

The editorial by Peter Hedera notes that spastin may have a microtubule-severing function, serving to regulate microtubule stability. There are more than 100 known SPAST mutations: missense, nonsense, small deletions/insertions, and splicing variants. The presence of many private mutations, the absence of known hot spots, and the lack of genotype/phenotype correlation has necessitated screening of the entire SPAST coding region with adjacent intronic segments. Despite this approach, SPAST mutations have not been demonstrated in 20% of families with clear linkage to the SPG4 locus. Beetz et al. provide an elegant solution to this vexing problem using a multiplex ligation-dependent probe amplification method. Mutation analysis of the SPAST gene should include a method for detection of aberrations of gene dosage.

see page 1912

Neuropathology across the Lewy body dementias

Ballard et al. evaluated the association between pathologic characteristics and duration of PD prior to dementia in dementia with Lewy bodies and PD dementia. Longer duration of PD was associated with less Alzheimer pathology and less cortical α-synuclein, but more severe cholinergic deficits.

see page 1931

The editorial by Lippa and Emre notes that patients with both PD dementia and DLB have Lewy body pathology in the nucleus basalis of Meynert, leading to cortical cholinergic deficits, which are greater than those seen in patients with AD. The Ballard et al. study adds to what we know about cholinergic losses in PDD and DLB by examining a range of patients with earlier, later, and late development of dementia. They show that PDD patients with longer histories of parkinsonism before dementia have more severe cholinergic losses, surprisingly with less severe cortical pathology in other respects. A clinical implication of this finding is that this subgroup may benefit from cholinergic treatment to a greater extent.

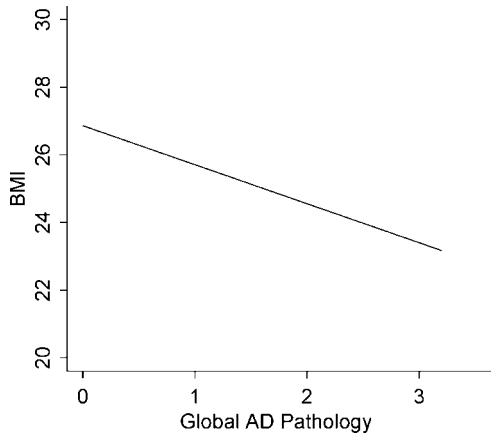
see page 1910

Body mass index and the risk of PD

In a prospective cohort study of 22,367 Finnish men and 23,439 women, Hu et al. examined the association between body mass index and the risk of PD. Excess weight, defined as a body mass index of 23 or more, was associated with elevated risk of PD among both men and women.

see page 1955

Body mass index in older persons is associated with AD pathology



Buchman et al. assessed body mass index proximate to death and quantified AD pathology in 298 deceased persons with and without dementia. Body mass index was associated with AD pathology regardless of dementia status, suggesting that loss of body mass index may be a consequence of the pathology of AD.

see page 1949

New-onset high blood pressure in acute ischemic stroke

Rodríguez-Yáñez et al. studied 844 patients with ischemic stroke to evaluate the outcome in different groups of patients according to blood pressure during acute phase (normotensive, chronic, and new-onset high blood pressure). The authors found that new-onset but not chronic hypertension was associated with poor neurologic outcome and with an inflammatory response.

see page 1973

Number of siblings and childhood nervous system tumors

In a study on the total population of Sweden, Altieri et al. found that children with a high number of siblings have a two- to threefold increased risk of childhood nervous system tumors, suggesting a possible role of childhood infections in the etiology of the disease.

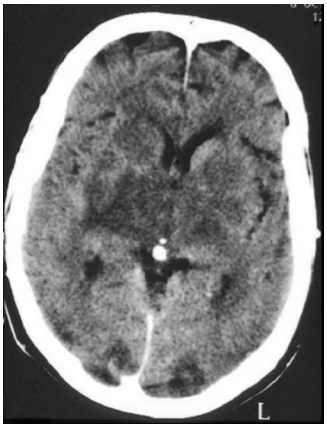
see page 1979

Brain metals in liver failure with pallidal MRI hyperintensity

Neurologic syndromes, including parkinsonism, occur in liver failure, associated with pallidal MRI T1 hyperintensity. In postmortem analyses, Klos et al. found that high pallidal manganese concentrations correlated with MRI hyperintensity. Manganese and copper are normally biliary excreted; both metals were selectively elevated in multiple other brain regions, and could contribute to other neurologic syndromes seen with liver failure.

see page 1984

Neurologic complications after hematopoietic cell transplantation



Toxoplasma encephalitis in a CD34$^+$ autologous HPCT recipient

In a study of 361 hematopoietic cell transplantation recipients, Denier et al. report symptomatic neurologic complications in 16% of the patients. Complications varied with the underlying disease and type of transplantation and were associated with poor survival rates.

see page 1990

Vitamin D therapy in patients with epilepsy

Mikati et al. compared the effects of two vitamin D doses over 1 year in 72 adults and 78 children on AEDs. The high dose (4000 IU/day) increased BMD in adults. Both doses (400 and 2000 IU/day) resulted in comparable increments in children.

see page 2005

Sepiapterin gene mutation in dopa-responsive disorder

Friedman et al. describe a woman with developmental delay, dopa-responsive movement disorder, and hypersomnolence with mutation in the sepiaterin reductase gene. Similar patients may benefit from dopaminergic and serotonergic therapies and should have CSF analysis to search for this treatable disorder of neurotransmitter metabolism.

see page 2032

fMRI brain changes in sensory conversion disorder

Using fMRI, Ghaffar et al. provide evidence of cerebral dysfunction in patients with sensory conversion disorder. Stimulation of an anesthetic limb failed to elicit activation in the contralateral somatosensory cortex. Instead, activation was noted in limbic areas such as the anterior cingulate and orbitofrontal cortex.

see page 2036

The editorial by Hurwitz and Prichard notes that the Ghaffar et al. report on fMRI findings in three patients with unilateral psychogenic sensory disturbance showed that as expected, unilateral vibrotactile stimulation activated primary sensory cortex (S1) contralateral to the normal, sensate limb. Unilateral stimulation of the insensate limb failed to activate contralateral S1, in keeping with the patients' anesthesia. In contrast, bilateral stimulation activated primary sensory cortex contralateral to the normal limb, but it also activated the previously dormant S1. Failure of S1 activation contralateral to the insensate limb with unilateral but not bilateral stimulation was thus a reversible functional disturbance. Bilateral stimulation may serve as a distraction, shifting attention, and thereby overcoming the inhibition S1. Their findings add to the growing body of data that implicates attention and active inhibition in the conversion process.

see page 1914

Retinopathy in primary CNS lymphoma survivors

Grimm et al. describe five long-term survivors of primary CNS lymphoma who developed retinopathy long after chemotherapy and whole brain radiation. Treatment-related retinopathy is probably underestimated and may be confused with ocular recurrence of lymphoma.

see page 2060

December 12 Highlights

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