Abnormal cingulum fiber structure in MCI and AD

Fractional anisotropy in the left posterior cingulum.

Using diffusion tensor imaging (DTI), Zhang et al. report structural alterations of cingulum fibers, which connect hippocampus and posterior cingulate gyrus, in subjects with mild cognitive impairment (MCI) and Alzheimer disease (AD). These alterations were better than conventional atrophy measurements in differentiating MCI and AD from normal aging.

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The editorial by Little and Holloway notes that although we can visualize and differentiate white and gray matter with standard MRI pulse sequences, they do not allow us to examine the integrity or directionality of white matter tracts. DTI takes advantage of the diffusivity of water and the restrictions imposed on the diffusion of water by white matter fiber tracts. In well-organized and intact white matter fiber tracts, water diffusion will occur preferentially along those tracts (i.e., be more anisotropic). When there is less organization or a lack of aligned and organized fiber structures (i.e., gray matter, CSF, axonal loss or demyelination), water diffusion will be more isotropic. The degree of alignment and anisotropy is commonly calculated as the fractional anisotropy. The exact reasons for the differences in water diffusion and mechanisms for underlying vulnerability of the white matter tracts are not yet fully understood in AD or in MCI, but could be related to ischemic changes, secondary axonal (wallerian) degeneration, or some type of primary white matter degeneration. DTI provides a method for identifying morphologic substrates or neuroanatomical correlates for disease progression. In addition, although investigations of underlying disease mechanisms will continue, the expression of these mechanisms on white matter fiber tracts (even if the mechanisms are not fully understood) provides fertile ground for prognostic and therapeutic research in vivo.

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Pilot study of coenzyme Q10 and GPI-1485 in PD

The NET-PD group's futility trial did not establish futility; this trial, their second pilot study, finds little to pursue for further investigation. The placebo group did better than expected and, when combined with other current studies, puts their prior results suggesting possible benefits of creatine and minocycline in a new perspective.

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Phenylbutyrate in spinal muscular atrophy

Mercuri et al. report a double-blind, randomized, placebo-controlled study in SMA type 2. The trial does not support the efficacy of phenylbutyrate at the regimen used in this study and highlights the need for placebo-controlled studies in SMA.

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The editorial by Kaufmann and Finkel notes that Mercuri et al. have confirmed that motor function assessments are feasible as the primary outcome in SMA trials. Although phenylbutyrate was not beneficial under the conditions of this study, a longer treatment period may be needed since rescuing neurons to measurably restore motor function may require an observation period beyond 13 weeks. Also, an alternative dosage or regimen might have been more effective. A phase 1 of phenylbutyrate study addressing some of the issues related to dose and regimen is under way in North America.

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Endurance training: A treatment for LGMD2I

Sveen et al. found that 12 weeks of moderate-intensity endurance training safely increased exercise performance in patients with limb-girdle muscular dystrophy type 2I (LGMD2I). The patients' maximal oxygen uptake and workload increased, muscle morphology and creatine kinase levels reflected no muscle damage, and self-reported questionnaires indicated better daily function after training.

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■ **Vertebral artery hypoplasia and posterior stroke**

Perren et al. studied 725 sequentially admitted first-ever stroke patients for vertebral artery hypoplasia. Vertebral artery hypoplasia was significantly more frequent in patients with posterior cerebral infarcts than in those with strokes in other vascular territories. Vertebral artery hypoplasia may be a predisposing factor in posterior circulation strokes.

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■ **A 34-year-old man with progressive behavioral and language disturbance**

In a new monthly feature, *Neurology* Clinical Pathological Conference, Dr. Bruce L. Miller discusses a case of a young man with a rapidly progressive cognitive and language impairment.

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