Nerve regeneration enhanced by NT-3 in CMT1A

NT-3 treated (A), regenerating axons in (A), untreated (B), and BDNF treated nude mice (C) at 8 weeks.

Sahenk et al. examined efficacy of NT-3 treatment in animal models and in a randomized controlled pilot trial in patients with CMT1A. NT-3 augmented axonal regeneration in the animal models, improved sensory scores of patients, and increased the number of small myelinated fibers in sural nerves.

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The editorial by Pleasure and Chance considers the mechanism by which NT-3 enhances regeneration of myelinated axons in CMT1A, a disorder affecting primarily Schwann cells. NT-3 improves axonal degenerative disorders caused by neurotoxins such as pyridoxine and cisplatin. It may exert its therapeutic effects primarily on neuronal perikarya or axons. If this is correct, NT-3 therapy may enhance axonal maintenance and regeneration in CMT1A by substituting for the lack of normal Schwann cell tropic support that results from the excess Schwann cell synthesis of PMP22 in these patients. Alternatively, since Sahenk et al. observed that NT-3 treatment increased the numbers of Schwann cells in both nude mouse CMT1A xenografts and in Trembler-J sciatic nerve segments distal to a crush, the therapeutic effect of NT-3 in CMT1A may be exerted primarily on Schwann cells. These exciting preliminary results in patients clearly justify a much larger, double-blind trial of NT-3 therapy in CMT1A.

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Dysphagia in unilateral medullary infarction

Using video-fluoroscopic swallowing tests, Kwon et al. compared dysphagia in 37 patients with lateral medullary infarction (LMI) and nine patients with medial medullary infarction (MMI). Dysphagia in LMI was usually related to reduced range of hyolaryngeal excursion whereas that in MMI was usually related to delayed timing.

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Effect of mitoxantrone on MRI measures in progressive MS

Krapf et al. examined the effect of mitoxantrone vs placebo in patients with worsening relapsing or secondary progressive MS over 24 months. Previous reports indicated that mitoxantrone delayed progression of disability and reduced relapse rates. The present study found no significant difference on the primary MRI measure, the number of MRI scans with gadolinium enhancement, though several secondary MRI measures showed a therapeutic effect. These results provide another example of discordance between effects on clinical and MRI measures of disease activity.

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LRRK2 gene in PD

Paisán-Ruiz et al. identified typical PD in three LRRK2 families (G2019S and I1371V) who presented with a variable age at onset that is not explained by APOE genotypes. The four common coding LRRK2 variations neither constitute strong PD risk factors nor modify the age at onset in a case-control dataset.

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Farrer et al. assessed the frequency of nine LRRK2 mutations in community-based PD from the midwestern United States. Of 2,140 subjects genotyped, 6 of 786 probands (0.8%) have a LRRK2 mutation.

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Zabetian et al. observed LRRK2 gene mutations in 6 of 371 (1.6%) consecutively recruited clinic patients with PD, including two with new putative pathogenic variants (R1441H, IVS31 + 3A@G).

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The editorial by Tatiana Foroud considers the genetic causes and risk factors for PD. In families with clear Mendelian inheritance, five genes have a confirmed role in PD etiology: alpha-synuclein (SCNA; PARK 1), parkin (PRKN; PARK2), PTEN-induced putative kinase 1 (PINK1; PARK6), oncogene DJ-1 (DJ-1; PARK 7), and leucine-rich repeat kinase 2 (LRRK2; PARK 8). Mutations in parkin cause early onset, autosomal recessive PD; heterozygous mutations in parkin may also act as a susceptibility factor, increasing the risk for PD. Important conclusions from these three articles include the following: LRRK2 mutations are more common among patients with a family history of PD vs those with sporadic disease; the clinical phenotype of LRRK2 positive patients is indistinguishable from those with a mutation. It remains unsettled what proportion of the 51 exons of LRRK2 need to be screened; the penetrance of LRRK2 mutations is incomplete.

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■ Mirror-like spread of chronic pain

Forss et al. demonstrated that mirror-like spread of chronic pain was associated with altered interhemispherical conduction in a patient with complex regional pain syndrome.

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■ Using a mirror to create a painful phantom

Acerra et al. found that in patients with CRPS1, stimulating the unaffected limb caused pain at the identical site in the affected limb, but only if patients watched the stimulation in a mirror.

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■ Distorted body image in complex regional pain syndrome

G. Lorimer Moseley manipulated photographs of both limbs in controls and people with CRPS. Patients consistently selected as accurate a photograph that showed their affected limb to be bigger than it is.

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The editorial by Birklein and Rowbotham on these three articles notes that there are symptoms that are not explained by peripheral posttraumatic mechanisms: CRPS after a trivial trauma, the CRPS movement disorder, and the spreading of CRPS symptoms to other extremities. All three of these studies suggest that central processing of sensory input, visual or tactile, must be altered in CRPS, in particular if the disease is not cured during the acute peripheral stages. They note the studies' limitations: investigator bias cannot be excluded; we do not know whether the findings are specific for CRPS, or simply reflect the result of chronic pain in body regions with extensive sensory representation in the brain. Weighing the pros and cons, the three studies together provide important information for our understanding of chronic pain. Earlier studies gave evidence for peripheral and spinal mechanisms of pain amplification. Additionally (not alternatively) we also now understand that pain is part of consciousness.

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■ The dangers of hand-held phoning while driving

Head ranges in the with phone vs without phone conditions.

Oommen and Stahl show that independent of distraction, hand-held phones suppress head movements, possibly reducing attention to the surroundings.

see page 754

■ Headaches in subacute angle-closure glaucoma

Shindler et al. identified that patients with subacute angle closure who had intermittent headaches were sometimes misdiagnosed as having migraine.

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■ Absence of BMAA neurotoxin in human brain

Montine et al. failed to detect BMAA, a neurotoxin implicated in ALS-PDC of Guam and AD, in frozen brain from patients and controls. Accumulation of BMAA in the brain does not explain these disorders.

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