idiopathic BV than in those with BV of known cause, and were associated with an increased prevalence of peripheral neuropathy. Hearing was impaired in 25% of the study group—most often in patients with BV caused by Cogan's syndrome, meningitis or Menière's disease.

These findings should be used to inform further research into this complex disorder. The data highlight the need for a combination of testing modalities for diagnosis and management of BV, and for care when prescribing certain medications, particularly ototoxic aminoglycosides.

Original article Zingler VC *et al.* (2007) Causative factors and epidemiology of bilateral vestibulopathy in 255 patients. *Ann Neurol* [doi: 10.1002/ana.21105]

Repetitive nerve stimulation is a clinically useful test for cramp–fasciculation syndrome

Cramp–fasciculation syndrome (CFS) has been suggested to be caused by hyperexcitability of peripheral nerves. Reasons for this hypothesis include an overlap in symptomatology of CFS and acquired neuromyotonia, and the fact that afterdischarges and cramp potentials following repetitive nerve stimulation (RNS) occur more readily in patients with CFS than in individuals without this condition. Conclusive evidence for this hypothesis, however, is lacking.

In a retrospective cohort study, researchers from Emory University, Atlanta, GA, examined peripheral nerve excitability in 108 consecutive patients who had been evaluated with posterior tibial RNS. Among this patient population, 36 individuals met clinical criteria for the diagnosis of CFS. RNS results were classified as normal or abnormal by two investigators on the basis of the presence or absence of afterdischarges, cramp potentials or continuous motor unit activity. At all stimulation frequencies (1, 2 and 5 Hz), abnormal RNS was significantly more frequent among those with CFS than among those without this syndrome ($P<0.002$ for all). The specificity of abnormal RNS for the diagnosis of CFS was highest (76%) when abnormal RNS was defined on the basis of afterdischarges, cramp potentials or continuous motor unit activity at 1 Hz; however, sensitivity was highest (83%) when abnormal RNS was defined on the basis of abnormalities at any frequency. Receiver operating characteristic curve analysis revealed that tibial RNS correctly classified CFS in 75% of subjects. These results indicate that CFS is a form of abnormal peripheral nerve excitability, and that RNS might be a clinically useful test for CFS.

Original article Harrison TB and Benatar M (2007) Accuracy of repetitive nerve stimulation for diagnosis of the cramp–fasciculation syndrome. *Muscle Nerve* **35:** 776–780

Extended hypoestrogenicity negates the neuroprotective effect of estrogen therapy

Ischemic injury is known to trigger an inflammatory response that contributes to brain injury. Many observational and retrospective studies in postmenopausal women have shown a neuroprotective effect of estrogen therapy (ET). Evidence indicates that this neuroprotective action might be attributable to estrogen's anti-inflammatory actions; however, neither the Women Estrogen Stroke Trial (WEST) nor the Women's Health Initiative (WHI) found any neuroprotective benefits associated with ET. Now, research conducted by Suzuki *et al.* has provided a potential explanation for the negative findings of these trials.

In this study, 19-week-old mice were ovariectomized and immediately implanted with capsules containing either oil or 17β-estradiol (E_2). A second group of mice underwent a period of hypoestrogenicity between being ovariectomized at 9 weeks of age and being implanted 10 weeks later with capsules containing either oil or E_2. All mice were subjected to ischemic injury at 20 weeks of age. Ischemic injury resulted in an increase in the production of the proinflammatory proteins monocyte chemoattractant protein 1 (MCP-1, or CCL2) and interleukin 6 (IL-6) on the injured side of the brain compared with the contralateral side. In comparison with oil-treated mice, mice implanted with E_2 on ovariectomy showed a significantly reduced upregulation of MCP-1 and IL-6 on ischemic injury. Notably, following hypoestrogenicity, E_2 was unable to attenuate ischemia-induced production of MCP-1 and IL-6. The authors conclude that a period of hypoestrogenicity prevents E_2 from exerting its anti-inflammatory actions. Many of the women participating in the WEST and WHI experienced hypoestrogenicity