temporal improvement during and after a flu-like syndrome. In July 1992 solo treatment with interferon-α-2a (Roferon-A) at a dosage of 3 million international units (MIU) twice weekly was begun. On the third day after the first injection a dramatic improvement was seen and during 11 days the patient progressively recovered to normal. Serial nerve conduction studies showed progressive reduction of conduction blocks. Seven days after the reduction of interferon-α to 1 MIU/week, progressive weakness of distal muscles occurred that paralleled an increase in multiple conduction blocks. Reinstatement of interferon-α-2a treatment at a dosage of 2 MIU twice weekly, produced a complete recovery within six days. Again the dose of interferon was gradually reduced to 1 MIU twice weekly, without clinical changes.

Only minor adverse effects, such as fever and arthralgias, were seen during interferon treatment.

Patient 2 was a healthy 3 year old boy who developed a waddling gait and muscle pain in his legs 20 days after an upper respiratory tract infection. The patient had recovered spontaneously after 15 days. During the next three months he had another three episodes of leg weakness lasting 10–15 days. Brain and spinal cord MRI was normal; electrophysiological studies showed delayed motor conduction velocity with multiple conduction blocks in all the nerves tested and normal sensory conduction velocities. The CSF contained 96 mg/dl protein and 3 white blood cells/ml, but no oligoclonal bands. During the fifth attack the child became unable to walk unaided and was admitted to our neurological department. He was treated with IV Ig at a dose of 1 g/kg daily for two days and prednisone (at a dose of 50 mg every other day) and after three days he regained the ability to walk. Neurography showed disappearance of conduction blocks in two of three motor nerves. Twenty days later the boy had another relapse. Again treatment with IV Ig improved motor symptoms in a few days. In the next 15 months he showed relapses every 13 to 20 days despite treatments with azathioprine and cyclosporin. All the episodes responded to IV Ig. During three relapses the patient was treated with plasma exchange and showed improvement comparable with IV Ig treatment. Treatment with interferon-α-2a (Roferon-A) (2-5 MIU/day) was given. After this treatment the child regained normal strength within 15 days. The dose of interferon-α was reduced to 2 MIU twice a week after three months. The patient showed no relapses during the subsequent months and no adverse effects were seen. Neurography performed two months after interferon treatment showed improvement of motor conduction velocity in all nerves with pronounced reduction of conduction blocks.

On the basis of the research criteria for the diagnosis of CIDP our patients were affected by "probable CIDP". Despite a good response to IV Ig, these patients were still moderately disabled and frequent infusions were needed. In 1992 Engel et al. described a patient with long lasting CIDP unresponsive to corticosteroids, azathioprine, cyclosporin, plasma exchange, and IV Ig, who showed pronounced improvement with interferon-α treatment. This finding led us to the use of interferon in our patients.

Interferon-α treatment resulted in a dramatic and long-term recovery. We doubt that this response was fortuitous, because (a) both patients showed a pronounced improvement a few days after starting interferon-α and this result was never achieved with other treatments; (b) no relapse occurred during full dosage interferon-α treatment whereas before this the patients had had a relapsing course over a long period, despite immunosuppressive treatments; (c) patient 1 deteriorated on reducing interferon-α to 1 MIU a week and promptly responded to a higher dose, suggesting a dose-response effect.

The mechanism by which interferon induced an improvement in our patients is uncertain. Interferons exert complex immunomodulator effects and there is evidence that interferon-α may both improve or worsen autoimmune disease. The recent finding that interferon-α may benefit patients affected by multiple sclerosis and that the production of lymphocyte interferon-γ is reduced by this treatment, suggests that interferons may play a central part in the pathogenesis of demyelination in both the central and the peripheral nervous system.

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Kava and dopamine antagonism

Kava is a drink widely used for its calming and tranquilising properties by the native population in the islands of the south Pacific. The beverage is prepared from the roots of the kava plant (Piper methysticum); besides in widespread social use and as a ceremonial drink, and heads of state have been reported to drink kava during welcome.
ceremonies in Fiji. Pharmacological preparations of kava are marketed in various European countries as mild anxiolytics (for example, Laitan or Kavasporal in Germany, Potter's antioxidant tablets in the United Kingdom, Viocava in Switzerland, Mosaro in Austria), and 547,000 units of preparations containing kava were sold in Germany during 1993. The basis of kava's action has been attributed to a group of α-carboline derivatives (dihydrokawain, kawain, dihydrokawain, methysticin, dihydroyangonin, yangonin) present in the root extract of the kava plant, but little is known about the pharmacological properties of these compounds.

We have recently seen four patients who developed clinical signs suggestive of central dopaminergic antagonism after exposure to various kava preparations.

Patient 1, a 28-year-old man, had a history of three episodes of acute dystonic reactions and exposure to promethiazine (50 mg in 1983) and fluphenazine injections (1.5 mg in 1984). Each time he had been treated for symptoms of an acute attack of involuntary neck extension with forceful upward deviation of his eyes, which had begun 90 minutes after the intake of the first dose of Laitan (100 mg kava extract) in 1984, and he presented spontaneously within about 40 minutes.

Patient 2, a 22-year-old woman, was prescribed Laitan (100 mg kava extract) because of anxiety and nervousness. Four hours after the first morning dose she experienced involuntary oral and lingual dyskinesia, tonic rotation of the head to the right, and painful twisting movements of the trunk. After about 45 minutes later 2.5 mg biperiden was given intravenously, and the dystonic reaction immediately subsided.

There was no history of any other drug exposure during the preceding month.

Patient 4, a 76-year-old lady, had first developed signs of idiopathic Parkinson's disease at the age of 59. After eight years of levodopa treatment motor fluctuations and dyskinesia were becoming an increasing problem. When first seen, she was taking 500 mg levodopa (plus 125 mg benserazide) per day and was experiencing motor fluctuations in the entrance room about one hour later, and 5 mg biperiden given intravenously immediately stopped the dyskinesia. The patient denied having taken any other medication during the preceding month.

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We hereby report abnormalities of lactate production only after muscular effort in asymptomatic carriers of LHON.

We studied 28 asymptomatic members of two unrelated Italian families with LHON. Family 1, with 14 members examined, had the np 11 778 mtDNA mutation only. Family 2 had the primary np 11 778 mutation plus the np 13 708 and 4216 secondary mutations. In all cases, blood, urinary epithelium, and hair were examined for mtDNA mutations according to described methods. Seven out of 14 members of family 1 and nine out of 14 of family 2 carried wild-type mtDNA. All carriers, members and non-carriers, were members of family 1 and family 2, whether carriers or non-carriers.

Our findings indicate that healthy carriers of 11 778 mtDNA mutations display abnormal lactate production only under conditions of muscular exercise. The lactate findings are thus in good agreement with our P-MRS studies of muscle again showing normal resting conditions but delayed recovery of phosphocreatine after exercise in affected patients and asymptomatic LHON carriers alike. They imply that LHON should be considered a threshold characteristic, and suggest that neurological dysfunction sets in when metabolic demands overcome the already impaired brain energy reserve. To explain the preferential involvement of neural structures, it is interesting to note that, whereas normal skeletal muscle operates at a resting rate of 16–19% of its maximal velocity of ATP biosynthesis (Vmax), brain resting rate of ATP synthesis is normally 55%, rising to 59–63% in LHON, much near its maximal energy capability, and thus also nearer to the theoretical threshold of energy failure. The reasons, however, for the preferential involvement of the optic nerve, although

findings of beneficial effects of kava on schizophrenic symptoms in Australian Aboriginals. Experimentally, kava extracts have been shown to antagonise stereotypies induced by apomorphine.1 We draw attention to the potential of extrapyramidal side effects of kava preparations and caution their use, particularly in elderly patients.

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