ceremonies in Fiji.¹ Pharmacological preparations of kava are marketed in various European countries as mild anxiolytics (for example, Laitan or Kavasporal in Germany, Potter's antigian 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 -pyrones (dihydrokavain, kawain, dihydromethysticin, methysticin, dihydroyangonin, yangonin) present in the root extract of the kava plant,² but little is known about the pharmacology of these various 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 promethacin (50 mg in 1983) and fluspirilen injections (1.5 mg in 1983 and 1986) for treatment of anxiety. Each time biperiden (5 mg intravenously) had led to immediate and complete relief of symptoms. He denied further use of these drugs when he presented at our hospital with a recent history 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 1993 and subsided 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 dyskinesiae, tonic rotation of the head to the right, and painful twisting movements of the trunk. 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 months.

Patient 3, a 63 year old woman, experienced forceful involuntary oral and lingual dyskinesiae of sudden onset after taking Kavasporal forte (150 mg kava extract) three times daily for four days because of anxiety. She was seen in the emergency room about one hour later, and 5 mg biperiden given intravenously immediately stopped the dyskinesiae. The patient denied having taken any other medication during the preceding months.

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 dyskinesiae were becoming an increasing problem. When first seen she was taking 500 mg levodopa (plus 125 mg benserazide) per day and was experiencing motor oscillations between Hoehn and Yahr stage III when "on" and stage V when "off".

Kavasporal forte (150 mg kava extract) twice daily was prescribed by her general practitioner because of complaints of inner tension. Within 10 days she noted a pronounced increase in the duration and number of her daily "off" periods. She returned to her normal baseline pattern within two days of discontinuing Kavasporal forte.

These case histories suggest that the sedative effects of kava might result from dopamine antagonistic properties of the extracts from the *Piper methysticum* plant. This possibility is also supported by clinical

findings of beneficial effects of kava on schizophrenic symptoms in Australian Aborigines.³ Experimentally, kava extracts have been shown to antagonise stereotypies induced by apomorphine in mice.⁴ 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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Abnormal lactate after effort in healthy carriers of Leber's hereditary optic neuropathy

Leber's hereditary optic neuropathy (LHON) is a maternally inherited disorder associated with several point mutations in mitochondrial DNA (mtDNA). It preferentially affects neural structures and the heart conduction system. The reasons for such preferential clinical expression, although they may relate in part to the different degree of organ heteroplasmy, are still imperfectly known. Expression of the mitochondrial defect depends on each tissue's differing metabolic requirements, being manifest only when a certain metabolic threshold is reached. Functional stress may therefore be required for expression. Skeletal muscles are clinically spared in LHON: symptoms and signs of muscular involvement are never detected and muscle biopsies usually lack ragged red fibres, the hallmark of mitochondrial myopathies.¹ Abnormalities in the form of subsarcolemmal rims of enlarged mitochondria may, however, be found on electron microscopy together with electron dense and paracrystalline inclusions.¹ A partial defect of the complex I of the respiratory chain has also been found in the muscle¹ and platelets² of patients with LHON.

We have shown that phosphorus magnetic resonance spectroscopy (³¹P-MRS) shows impaired recovery of phosphocreatine after exercise in the muscles of patients affected with LHON with the 11 778 mtDNA mutation, in the absence of resting abnormalities³; we also have evidence that the same occurs in asymptomatic carriers.

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.³ Seven out of 14 members of family 1 and nine out of 14 of family 2 carried the mtDNA mutation(s). All carriers were virtually homoplasmic for the mtDNA mutations, except one person from family 1, with a 5-25% of wild type mtDNA. All members, carriers and non-carriers, were examined by us and found to be clinically normal.

Serum lactate was evaluated at rest and after standardised moderate exercise on a cycle ergometer, according to the method of Nashef and Lane.⁴ Venous samples were collected at rest, immediately after 15 minutes of pedalling an electronically braked bicycle ergometer under ECG monitoring at the predicted heart rate, and 15 minutes after the end of exercise. Samples were collected without stasis in sodium fluoride containers and the plasma was immediately separated, frozen, and analysed (Lactic acid, DIMENSION®). A Student's *t* test on unpaired data was used to compare the two groups: carriers *v* non-carriers of the mtDNA mutation(s). Serum lactate concentrations at rest were comparable in both carriers and non-carriers. Lactate was significantly increased immediately after exercise and 15 minutes after recovery from exercise in the carrier group (table). No significant differences were found between 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 ³¹P-MRS studies of muscle again showing normal resting conditions but delayed recovery of phosphocreatine after effort in affected patients³ and asymptomatic LHON carriers alike. They imply that LHON should be considered a threshold character, 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 (V/Vmax%), brain resting rate of ATP synthesis is normally 55%, rising to 59-63% in LHON, much nearer to 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

Lactate concentrations (mean (SD)) mmol/l at rest, immediately after effort and 15 minutes after recovery in healthy carriers and non-carriers of LHON mtDNA mutation

	Rest	After effort	Recovery
Healthy carriers (n = 16)	0.99 (0.6)	2.63 (1.2) p<0.05	1.62 (0.8) p<0.04
Non-carriers (n = 12)	0.90 (0.4)	1.76 (1.0)	1.11 (0.4)

they may relate to the high frequency of the 11 778 mutant allele in the retinal cell layer and optic nerve,⁵ are still unclear.

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Painless ischaemic lumbosacral plexopathy and aortic dissection

There is only one case report dealing with ischaemic lumbosacral plexopathy without simultaneous signs of limb ischaemia.¹ We present a similar case characterised by the total absence of pain.

A 69 year old man suddenly developed a weakness and a numbness of the right leg. He also complained of vague abdominal discomfort but no pain was felt in the leg. His risk factors included arterial hypertension and angina pectoris. He was not diabetic. Neurological examination showed a pronounced global weakness (grade 0-2/5) of the right lower limb, including the hip flexors and the gluteal muscles. The knee jerk and the ankle jerk were abolished. Sensory disturbances were found below the L2 level on the right side. Light touch and proprioception were clearly impaired whereas sensation for pain and temperature was less diminished. No bladder dysfunction was noted and defecation was normal. Distal pulses were normal and there were no signs of muscle or skin necrosis. His CSF was normal. Aortic angiography showed a thoracoabdominal dissection extending from the origin of the descending thoracic aorta down to the bifurcation (type 3). The angiogram of iliac and femoral arteries and of distal arteries of lower limbs was normal.

An EMG taken two weeks later showed almost no voluntary motor unit potentials in the iliopsoas, quadriceps, glutei and thigh adductors muscles. Recruitment of motor units was much reduced in other muscles of the right lower limb. Fibrillations and positive sharp waves were absent. Nerve conduction studies showed absent right sural

and superficial peroneal sensory responses and low amplitude right posterior tibial and peroneal motor responses.

The patient had hypotensive treatment in the intensive care unit but dissection extended to the ascending aorta causing haemopericardium and the patient died four weeks later. A necropsy was not performed.

Our patient probably had an acute ischaemic plexopathy. The sudden beginning of the clinical picture "like an apoplexy" was in favour of a vascular aetiology. The diagnosis of more distal neuropathies was not suspected as an angiogram of the arteries of the lower limbs was strictly normal. Ischaemic neuropathies are divided into those occurring with diseases affecting large arteries and those occurring with diseases, such as diabetes, that affect small arteries. Acute ischaemia of peripheral nerves generally results from occlusion of a main proximal limb artery or from occlusion of many distal arteries. The rareness of such neuropathies can be explained by the relative resistance of peripheral nerves to ischaemia. It results from their slight metabolic needs (oxygen requirement of human nerve = 0.3 ml/100 g) and from their rich vascularisation, which provides a generous blood flow (43 ml/100 g/min).² The nutrient arteries that supply peripheral nerves enter the epineurium and form a collateral vascular network of inter-fascicular arteries along the length of the nerve, so that it is difficult to infarct a peripheral nerve. The intensity of nerve damage varies with the number of nutrient vessels, the availability of the collateral circulation, age, and the importance and particularly duration of arterial occlusion.

The different fibres that constitute peripheral nerves seem to be altered selectively by ischaemia. In some studies, anoxia seems to affect the small fibres before the large ones and Schwann cells seem to be more resistant to anoxia than axons. Nevertheless, opposite data are found in other studies, which suggest a greater vulnerability of large fibres.

Clinical features of ischaemic neuropathy are generally stereotyped.³ Sensory deficits are more frequent than motor deficits. In particular, patients develop deep burning pain and neurological examination usually shows impairment of all sensory modalities or pattern of sensory loss that spares the large fibres. There are no signs of muscle necrosis. An EMG usually shows abnormalities consistent with axonal damage. Conduction blocks are unusual.

Such ischaemic lumbosacral plexopathies have been reported after aortobifemoral graft and aortofemoral bypass graft by resection of nutrient arteries, after use of an intra-aortic balloon, and after vasospasm caused by an injection of drugs into an inferior gluteal artery. Only one case of painful ischaemic lumbosacral plexopathy due to an aortic dissection has been reported.¹

Anatomically, the lumbosacral plexus is supplied by five lumbar arteries, which originate from the abdominal aorta, the deep circumflex iliac artery, a branch of the external iliac artery, and the iliofemoral and gluteal branches of the internal iliac artery.⁴ In our patient, ischaemia of the lumbosacral plexus could be due to interruption of blood flow through the lumbar segmental arteries and branches of the iliac arteries secondary to the dissection of the aortic

artery walls and of the most proximal iliac artery walls just below the aortic bifurcation.

The clinical picture in our patient was also characterised by the absence of pain whereas causalgia like burning is generally common in acute and chronic ischaemic neuropathies.

Absence of pain has rarely been reported in ischaemic plexopathies. Clinical and pathological studies of nerves in painful neuropathies have been limited but the occurrence of pain is usually related to a selective damage of unmyelinated and myelinated small fibres. In the same way, painless neuropathies seem to be related to a selective damage of large fibres, as in our patient. On the other hand, a selective loss of fibres has not been confirmed by other studies, in which the ratio between large and small fibres was not modified.⁵

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Electroconvulsive therapy for the physical signs of Parkinson's disease without depressive disorder

Faber and Trimble¹ have reviewed the reports on electroconvulsive therapy (ECT) in Parkinson's disease. We conducted a prospective open trial to evaluate the short term benefit of ECT on the physical signs of Parkinson's disease without major depressive disorder. This was a repeated measures time series design where all patients received a single baseline assessment before and two assessments after ECT, and were their own control group. Four sessions of ECT were given unilaterally to the non-dominant hemisphere over eight days. Approval for the study was given by the ethics committee, Royal Hobart Hospital and all patients gave written informed consent.

Fifteen patients (12 men) participated. Five failed to comply with all assessments and were therefore eliminated from the analyses. The remaining population (seven men and three women) had an average age of 64.8 years. The time since initial diagnosis of Parkinson's disease ranged from two months to 16 years. Most were severely