LETTERS TO THE EDITOR

Marijuana for Parkinsonian tremor

In the late nineteenth century cannabis was often prescribed for Parkinsonian tremor, apparently with benefit.[1] Marijuana is known to contain several active substances with multiple properties and these include psychotropic, hypnotic, tranquillising, antiemetic, anticonvulsant and analgesic actions. The most potent constituent is thought to be tetrahydrocannabinol (THC) and its hedonic properties have long been exploited for recreational purposes.

One of our patients whose severe Parkinsonian tremor was resistant to medications including anticholinergics and beta-blockers claimed that she had obtained dramatic relief after smoking marijuana on three separate occasions, with benefit lasting up to three hours. We attempted to verify this claim by comparing the effects of marijuana with more conventional agents.

Five patients with idiopathic Parkinson's disease, and severe tremor were studied; all had previously been unresponsive to anticholinergics; levodopa, bromocriptine and beta-blockers had been tried in 4, 3 and 2 cases respectively. All patients were given on consecutive days: 1) marijuana smoked as a cigarette, 2) diazepam 5 mg orally, 3) levodopa/carbidopa 250 mg/25 mg orally (Sinemet 275), 4) apomorphine 1·5 mg subcutaneously. All drugs were given in the morning after withdrawal of normal medication overnight, and in the case of the levodopa on an empty stomach. Before administration of apomorphine, patients were given domperidone, a peripheral dopamine antagonist, to prevent side effects of nausea and hypotension. The marijuana was prepared as a cigarette containing approximately 1 g of the shredded leaf (2·9% THC by weight). Patients were assessed for Parkinsonian disability before and at intervals after dosing using a modified Webster scale;[2] particular care was taken in assessing tremor and the patients' subjective assessment was recorded.

None of the patients, including the woman who had previously reported benefit, experienced relief or demonstrated improvement of tremor following marijuana, despite central effects as evidenced by drowsiness or mild euphoria; no effects other than drowsiness and in two cases mild unsteadiness occurred after diazepam. However, in all five, similar improvement was seen after both levodopa and apomorphine, and in three cases tremor resolved completely.

These results do not support the notion that cannabis when smoked reduces tremor or any other Parkinsonian disabilities. The drug clearly has other effects and it may be that its non-specific sedative or anxiolytic actions benefit certain tremulous patients when anxiety is a significant trigger factor.

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1 Gowers WR. *A manual of diseases of the nervous system, vol II.* London: Churchill, 1888: 589–607.
2 Kempster PA, Frankel JP, Bovingdon M, *et al.* Levodopa peripheral pharmacokinetics and duration of motor response in Parkinson's disease. *J Neurol Neurosurg Psychiatry* 1989;52;718–23.

Unilateral cerebellar damage in focal epilepsy

We previously described reversible cerebellar diaschisis in a 20 year old woman with idiopathic focal motor seizures.[1] Her epilepsy started at the age of 13, becoming more severe in her late teens. At that time she was having motor seizures every few minutes, beginning on the left side of the face, spreading to the left arm and the left leg, and leading to secondary generalisation on average once per day. Her seizure frequency, usually five to 10 per day with secondary generalisation once per week, had been gradually increasing for six days. She had had four less severe episodes of poor control in the previous two years. Single photon emission computed tomography (SPECT) carried out during a seizure showed hyperperfusion (and therefore likely hypermetabolism) at the site of the focus and in the contralateral cerebellar hemisphere (fig 1a). The cerebellar hyperperfusion had disappeared four days later when the patient's seizures were under control. We suggested that secondary activation might be involved in the pathogenesis of cerebellar damage in severe epilepsy.

Since that time control of the patient's epilepsy has deteriorated, with increasingly prolonged and frequent episodes of simple partial status, despite therapeutic levels of phenytoin and phenobarbitone. She has become increasingly ataxic following periods of poor seizure control, and when drug levels are elevated above the target range. When present, the ataxia is worse on the left side, and is accompanied by nystagmus on left lateral gaze.

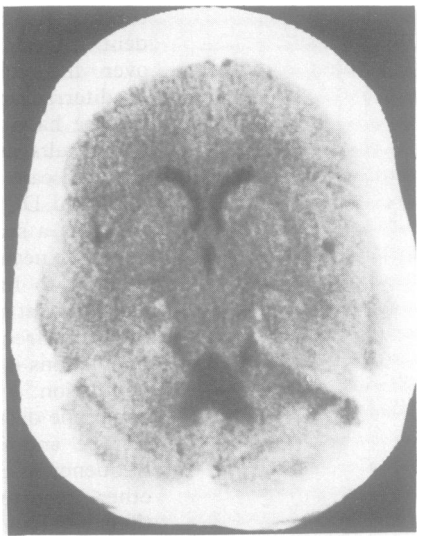

Figure 2 CT scan showing atrophy of the left cerebellar hemisphere, corresponding closely with abnormally perfused area on SPECT.

CT carried out in 1989, 20 months after the original SPECT scans, showed atrophy of the left cerebellar hemisphere (fig 2) which was not present in 1986. Magnetic resonance imaging (MRI) also showed the atrophy and showed the left cerebellar hemisphere as hyperintense on T2 weighted sequences and hypointense on T1 weighted sequences. Interictal SPECT showed hypoperfusion of a wide area of the right cerebral hemisphere, and of the left cerebellar hemisphere (fig 1b). Only the former feature was present on the original SPECT.

We originally demonstrated contralateral cerebellar activation in association with focal motor seizures and have now demonstrated developing neurological damage in the activated cerebellar hemisphere. This may have followed the episode of poor control preceding the first SPECT scan, but it seems more likely to have followed a number of her later episodes which were more severe and prolonged.

Cerebellar damage may be due to anticonvulsants, but in that case is usually bilateral. Brain and plasma phenytoin levels equilibrate

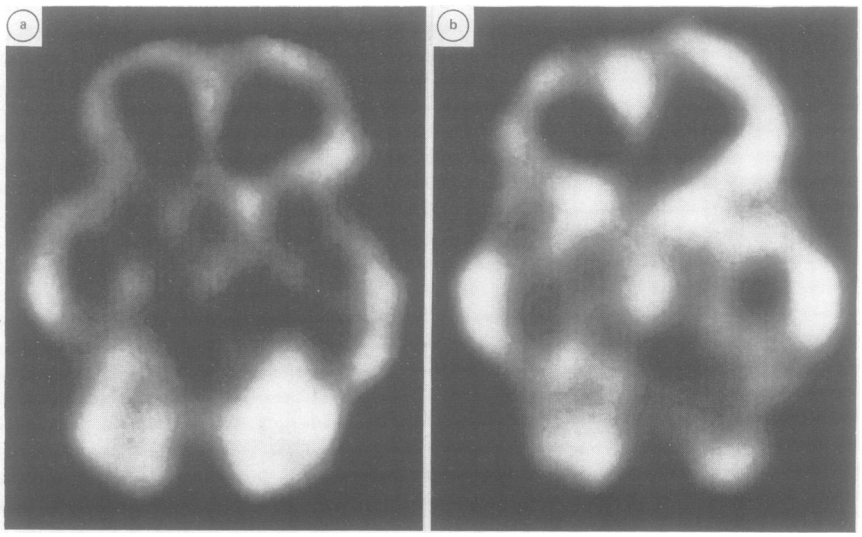

Figure 1 (a) Original ictal SPECT showing hyperperfusion of the left cerebellar hemisphere. (b) Recent interictal SPECT showing hypoperfusion of the left cerebellar hemisphere, corresponding closely with the originally hyperperfused area.