Marijuana for Parkinsonian tremor

In the late nineteenth century cannabis was often prescribed for Parkinsonian tremor, apparently with benefit. Marijuana is known to contain several active substances with multiple properties and these include psychotropic, hypnotic, tranquillising, antiepileptic, 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 3, 4 and 2 cases respectively. All patients were given on consecutive days: 1) marijuana smoked as a cigarette, 2) diazepam 5 mg orally, 3) levodopa, 375 mg orally (Sinemet 750), 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; 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 antispasmodic actions benefit certain tremulous patients when anxiety is a significant trigger factor.

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Unilateral cerebellar damage in focal epilepsy

We previously described reversible cerebellar diaschisis in a 20 year old woman with idiopathic focal motor seizures. 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 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 phenobarbital. She has become increasingly atactic 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 1 (a) Original ictal SPECT showing hyperperfusion of the left cerebellar hemisphere. (b) Recent interictal SPECT showing hyperperfusion of the left cerebellar hemisphere, corresponding closely with the originally hyperperfused area.
rapidly. This makes it unlikely that increased local blood flow will result in increased tissue concentrations in the steady state, though there is the possibility of an effect where frequent intravenous injections result in rapidly rising plasma levels. In 1987 our patient had three intravenous injections of phenytoin, two of 200 mg and one of 300 mg, but not before or since. While acute ischaemia can cause hyperperfusion, this usually persists long beyond the four days between the original SPECT scans.

Cerebral and cerebellar damage in association with seizures may be due to hypoxia, whether respiratory or due to hyperventilation, or relative, due to the high metabolic demand of the brain tissue involved in the seizure. More recent work has shown that pathological changes thought to be due to hypoxia can occur where brain oxygenation and perfusion is adequate, and positron emission tomographic (PET) studies have shown that perfusion and oxygenation of discharging epileptic foci is adequate for their metabolic demands. Meldrum proposed that sustained neuronal overactivity in itself may lead to neurological damage, whether widespread or localised (as in mesial temporal sclerosis), and there is evidence that glutamic acid, an excitatory neurotransmitter with neurotoxic properties, may mediate the effect.

This case demonstrates structural and functional damage in an area only secondarily activated by the epileptic discharge, and supports the concept that neural damage in epilepsy is partly or wholly due to neural overactivity.

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Syringomyelia with spontaneous resolution

Patients with syringomyelia have a range of physical and neurological symptoms and signs which usually progress gradually with occasional abrupt exacerbations in some patients and involves long periods without change. The size and the shape of the syrinx can be shown by CT myelography and/or MRI to vary during a follow up period of many years. Operation may reduce the size in some cases, but patients treated surgically sometimes show recurrent enlargement of the syrinx. On the other hand, spontaneous disappearance of the syrinx is not well documented. We report a case of syringomyelia with spontaneous resolution.

A 16 year old right handed boy was seen at our outpatients clinic in August, 1986 with numbness of the left side of his chest and upper limb. He was born at full term by normal delivery. At the age of 11 years, he slipped and fell down a flight of stairs, resulting in a pain on the left side of his back which lasted for a few weeks. The following year he was thrown down and fell on his back while playing Judo at school; he felt a tinging and lancinating pain in the left side of his chest and back. Following this episode, he started to experience similar pain during exercise. Several months later he noticed hypalgasia and hypoesthesia of the left side of his chest; this spread to affect the whole of the left arm.

In April 1985, aged 13, we examined him for the first time at another hospital. Positive neurological findings at that time included equivocal weakness of extension of the left fingers, areflexia of the left arm, hypereflexia of both legs, bilateral extensor plantar responses and dissociated sensory disturbance over the left C3–T7. CT myelography of the cervical cord revealed definite delayed uptake of the contrast material into the left dorsal parts of the spinal cord, consistent with a syrinx. In April 1986 he complained of a lancinating pain in his left finger radiating from his neck, when he sneezed, coughed, or strained at stool. On 28 July 1986, MRI (0-15 Tesla) was performed. There was a syrinx from C2 to T9 near the left dorsal column, as well as a Chiari malformation of Type 1 (fig 1a). He was referred to our clinic on 1 August 1986. Neurological examination at that time showed a slight weakness of the left finger extensor, abductor and adductor, diminished left hand grasping power (right 28 kg, left 16 kg), loss of upper and middle abdominal reflex with diminution in the lower part, and dissociated sensory disturbance over left C2–T9. Sweating was absent on the left arm and chest. He had bilateral extensor plantar responses.

In September 1988 (aged 16), the patient was evaluated at our clinic again. He did not complain of any weakness or pain. Neurological examination revealed some changes. His muscle strength was full throughout. His hand grip power was 33-0 kg (right) and 30-5 kg (left). He showed areflexia of his left arm and hyperreflexia of both legs. He did not have extensor plantar responses. Dissociated sensory disturbance was observed from C2–L1, but the degree was less than previously. MRI (1-5 Tesla) was performed on 10 November 1988 (fig 1b). On a T1 weighted image we could find neither a Chiari malformation nor any abnormal intensity in the

Figure 1a 1st MRI of whole spinal cord (left): TR = 500 TE = 40 sagittal, right: TR = 500 TE = 30 axial image showing a Chiari malformation and syrinx in the spinal cord.

Figure 1b 2nd MRI (left): TR = 1000 TE = 15 sagittal, middle: TR = 600 TE = 15 Axial image, reveals neither a Chiari malformation nor syrinx in the spinal cord. However, TR = 3300 TE = 90 T2-weighted images in the right of the figure showed a high signal intensity area in the spinal cord, indicating the previous location of the syrinx.