(35 minutes *v* 195 minutes respectively), a finding which might be explained by the differences in absorption of apomorphine from the two preparations.

These preliminary results suggest that apomorphine is effective when administered rectally as an enema and may be the chosen method for rapid relief of "off period" symptoms when other routes may be unavailable due to adverse effects or the patients' difficulty in applying subcutaneous or intranasal apomorphine. We advise regular proctoscopy when treatment is frequent or prolonged.

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HAM/TSP attributable to blood transfusion

A multi-centric case-control study was carried out to clarify possible environmental factors related to the onset of HTLV-I-associated myelopathy[1]/tropical spastic paraparesis[2] (HAM/TSP) in northern Kyushu, Japan, which comprises one of the most prevalent areas of HTLV-I in the world.[3]

The frequencies of blood transfusion before the onset of HAM/TSP were 33% (6/18) among male patients and 18% (12/67) among female patients, which were significantly higher than 8% in males and 9% in females in the general population. The age-adjusted summary odds ratios with 95% confidence intervals were 7·0 (2·9–17·0) for males and 2·4 (1·3–4·5) for females. The percentages of population attributable risk[4] of HAM/TSP attributable to transfusion were estimated to be approximately 29% (5–52) for males and 11% (1–21) for females.

The fraction of HAM/TSP attributable to transfusion after the introduction of blood screening for HTLV-I, in effect since 1986 in Japan, was definitely smaller than that before the programme. Our observations seemed compatible with a marked decline in newly diagnosed HAM/TSP patients after its introduction,[5] which may be part of the benefit of blood screening. Neither smoking nor drinking was related to the risk of HAM/TSP.

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Suppression of motor neuron firing by transcranial magnetic stimulation in a patient with multiple sclerosis

Transcranial magnetic stimulation produces a short latency excitatory response in tonically active single motor units in small hand muscles.[1 3] This is shown by a peristimulus time histogram, which cross correlates motor unit firing times with the time of the stimulus. The excitatory response in the first dorsal interosseous muscle (FDI) occurs at 20–30 ms and is termed the primary peak (PP); in some motor units a secondary peak at 50–90 ms is also seen.[3] PP is characteristically followed by a compensatory period of zero firing probability, which reflects the advancement of discharges that would have occurred shortly after PP had no stimulus been applied. Complete suppression of firing in response to transcranial magnetic stimulation in the absence of an excitatory peak has not been reported. The response of 21 single motor units to transcranial magnetic stimulation has been recorded in nine patients with multiple sclerosis (MS), to study the neural mechanism of symptoms caused by upper motor neuron lesions.[3] Findings have suggested that spatial and temporal summation at the spinal motoneuron is impaired by a reduction in the velocity and synchronisation of central transmission. For healthy subjects, however, complete suppression of tonic activity in single motor units by transcranial magnetic stimulation was not observed.

The patient, a 48 year old female, initially presented in 1986 with paraparesis, weakness affecting the left arm, and diplopia. The diagnosis of MS was supported by the finding of oligoclonal bands in the CSF, enhancing white matter lesions on CT and by delayed VERs. She was subsequently free of symptoms for four years. She then re-presented with pyramidal weakness of the right arm [reducing the power of the right FDI to 4/5, MRC scale], increased tone in the left leg, extensor plantar responses and impaired joint position sense in the toes. During this clinical episode the response to transcranial magnetic stimulation of three voluntarily activated low threshold motor units from the weakened right FDI was recorded.

The patient was right handed and gave her informed consent to the experiments which were performed with the approval of the local ethics committee. The inducing current flowed in an anticlockwise direction through a circular (Novametrix 200) positioned tangentially at the vertex. Single MU potentials were recorded using fine concentric needle electrodes (Dantec type 13L58). The patient was asked to maintain repetitive motor unit firing and was aided by auditory and visual feedback of the motor unit discharge. Signals were amplified with a band pass of 32 Hz to 16 KHz (Medelec type MS6) and epochs of −250 to +250 ms relative to the stimulus were digitised at 10 kHz (Cambridge Electronic Design 1401) for subsequent analysis. Up to 120 stimuli were given for each motor unit, delivered at random with respect to the

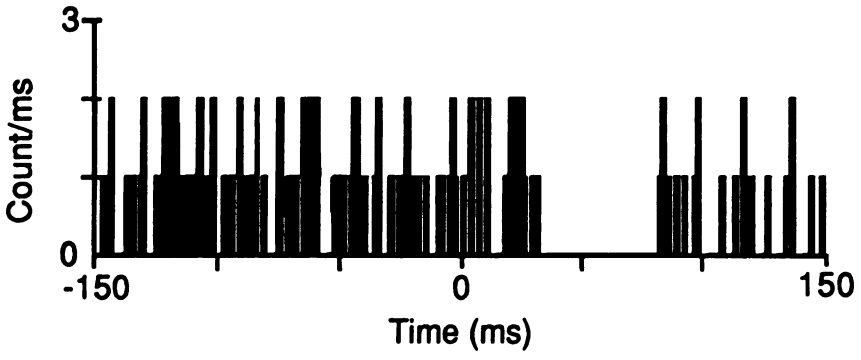

Figure Peristimulus time histogram constructed from the discharge of a single tonically active motor unit from FDI, recorded with a concentric needle electrode. Magnetic stimuli were delivered at time = 0, in 120 trials. There is a distinct period of zero firing probability with an onset latency of 34 ms and a duration of 47 ms. No excitatory peak is seen.

ongoing spike train. The rate of stimulation was less than once in 3 seconds. The stimulus intensities used were in the range of 60–70% of the maximal output of the stimulator, which was 12–15% lower than the threshold intensity for a compound muscle action potential recorded over the right FDI.

Peristimulus time histograms constructed off line demonstrated periods of zero firing probability for all three motor units. These had onsets after the stimulus of 34, 40 and 50 ms and durations of 47, 33 and 34 ms, respectively (fig). Neither primary nor secondary peaks were evident in any motor unit. The absence of any significant excitatory response was confirmed by cusum analysis.

In this patient motoneurons were suppressed from firing by motor cortical stimuli. This contrasts with the characteristic short latency excitation evoked by transcranial magnetic stimulation in the motoneurons from healthy subjects. The mechanism for this may have involved a transient withdrawal of excitatory drive, or there could have been an active inhibition of the motoneuron, either pre- or post-synaptically, from a pathway activated by the motor cortical stimuli. The findings suggest that this patient's weakness could be attributed in part to this suppression.

It is becoming clear from studies of the unitary response to transcranial magnetic stimulation[4 5] that the disabilities caused by upper motor neuron lesions can involve several mechanisms, including abnormalities of spatial and temporal summation at the motoneuron and also, we now believe, suppression of motoneuron firing via a central mechanism.

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Control of epilepsia partialis continua and secondarily generalised status epilepticus with isoflurane

The majority of patients with status epilepticus can be adequately controlled with conventional drugs including benzodiazepines, phenytoin and phenobarbital, but some require more aggressive therapy.[1] Various approaches have been used, most commonly general anaesthesia with continuous thiopental or pentobarbital infusion. Continuous infusions of diazepam, lidocaine, paraldehyde and more recently, etomidate and propofol have also been used. General anaesthesia using volatile agents such as halothane or isoflurane has been advocated in patients who are either refractory to parenteral therapy or experience unacceptable side effects from anticonvulsant drugs.[1 2] We report a patient whose status epilepticus and epilepsia partialis continua were controlled with the inhalational anaesthetic, isoflurane.

A 30 year old woman had a six year history of increasing simple partial, complex partial and secondarily generalised seizures from the left hemisphere. A left posterior temporal corticectomy performed four years after onset of seizures did not result in any significant clinical improvement. Pathology showed mild gliosis. Two months before admission, despite high doses of carbamazepine, valproic acid and clobazam, she developed epilepsia partialis continua with constant twitching of the right face, progressive right hemiparesis and dysphasia. EEGs revealed multifocal spikes and frequent seizures in the left hemisphere. MRI showed postoperative changes in the left posterior temporal region. When she began to have three to five secondarily generalised seizures an hour as well as the epilepsia partialis continua of the right face, additional administration of parenteral diazepam, phenytoin, phenobarbital and paraldehyde failed to control the seizures. She was transferred to the intensive care unit, intubated and ventilated using a Narkomed 2A anaesthetic machine and "circle" breathing system. Inspired gas was a mixture of oxygen and air to maintain an arterial oxygen saturation >96%. Positive pressure ventilation with 5 cm PEEP was adjusted to maintain normocapnia. Isoflurane was added to the fresh gas flow as required to control seizure activity and the end tidal concentration was monitored in conjunction with end tidal carbon dioxide. Other monitors included inspired oxygen concentration, intra-arterial blood pressure, high pressure and disconnect alarms on the ventilator. Small doses of morphine but no muscle relaxants were used following intubation with succinylcholine. The initial end tidal concentration of isoflurane was 0·5% which resulted in immediate clinical control of the sizures and marked EEG improvement (figure). Phenytoin and phenobarbital were continued at doses to produce therapeutic serum concentrations but other anticonvulsants were stopped. Twenty four hours after the isoflurane was administered, she had several short lived focal seizures and the concentration was increased to 0·7%. Another EEG showed no siezure activity. After 48 hours, the isoflurane was discontinued and the patient awoke within 15 minutes at a measured end tidal concentration of between 0 and 0·2%. She was extubated six hours later and transferred back to the ward the following day. She was maintained on phenytoin and phenobarbital and continued to have numerous daily focal seizures of the right face but only occasional generalised seizures. After a second corticectomy of the left lower rolandic region, seizures were focal, brief and less than 10 a week. Chronic encephalitis was found pathologically.

This is the second patient with status epilepticus we have successfully treated with isoflurane anaesthesia, and the first with epilepsia partialis continua. The other patient has been previously reported as one of a small series of similar cases from North America.[2]

The use of isoflurane anaesthesia has advantages over barbiturate coma which is the most commonly recommended "last resort" therapy for status epilepticus. The time to awaken after barbiturate coma is often several days due to the prolonged metabolism of the barbiturates, whereas our patient awoke within 15 minutes after 48 hours of isoflurane anaesthesia. The recovery time from inhalational anaesthesia depends mainly on the concentration used, the duration of use and the tissue solubility of the agent. As isoflurane is the least soluble of the currently available volatile anaesthetics, recovery from anaesthesia is more rapid. Other advantages include a lack of metabolic side effects and, unlike halothane, there is no evidence to date of hepatotoxicity. Renal toxicity from inorganic fluoride production does not appear to be a problem, which is a significant advantage over enflurane or methoxyflurane. Overall metabolism of isoflurane amounts to only 0·17% of the absorbed dose.[3]

The use of isoflurane is not without potential risks. Hypotension requiring vasopressor treatment is a common problem with prolonged anaesthesia using barbiturates or inhalational agents. Although hypotension was not a problem in our patient, treatment with a vasopressor agent is often required

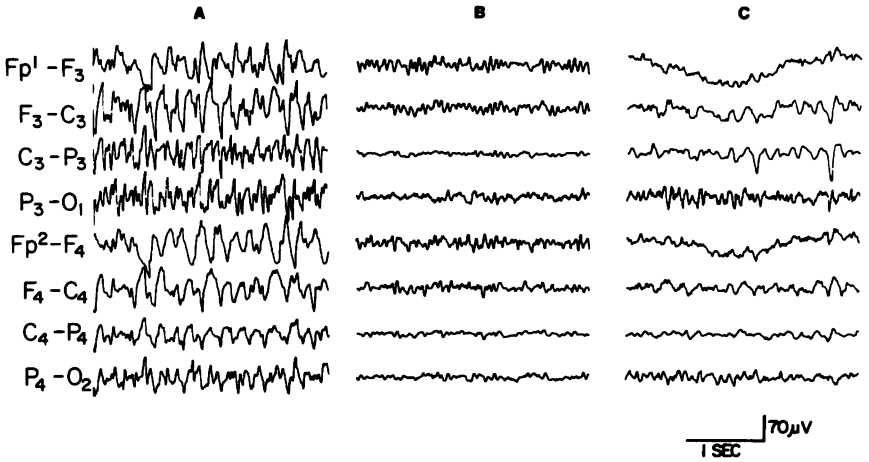

Figure EEG before (A), during (B) and following (C) treatment with isoflurane.