

## CASE REPORTS

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## Electroencephalographic Evidence of Seizure Activity under Deep Sevoflurane Anesthesia in a Nonepileptic Patient

Ian J. Woodforth, M.B., B.S., F.A.N.Z.C.A.,\* Richard G. Hicks, M.Sc.,† Matthew R. Crawford, M.B., B.S., F.A.N.Z.C.A.,‡ John P. H. Stephen, M.B., B.S., F.R.A.C.S., F.R.C.S.,§ David J. Burke, M.D., D.Sc., F.A.A., F.R.A.C.P.||

SEVOFLURANE suppresses central nervous system (CNS) background activity, but in animal experiments, deep anesthesia activates the electroencephalograph (EEG).<sup>1</sup> It has neurophysiologic properties similar to enflurane and increases the EEG and somatosensory-evoked potential (SEP) responses to high-frequency electrical stimulation of the skin or brain stem.<sup>1</sup> In addition, EEG evidence of seizure activity during deep sevoflurane anesthesia has been seen in patients known to have epilepsy.<sup>2</sup> We report the occurrence of typical spike-and-wave electrical seizure activity in the EEG of a patient anesthetized with 7% sevoflurane, without evidence of a clinical seizure.

### Case Report

An 11-yr-old girl suffering from idiopathic scoliosis was admitted for spinal fusion and internal fixation. She weighed 33 kg;

\* Visiting Anesthetist.

† Scientific Officer.

‡ Staff Anesthetist.

§ Visiting Orthopedic Surgeon.

|| Professor of Neurology.

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Address reprint requests to Professor Burke: Prince of Wales Medical Research Institute, High Street, Randwick, NSW 2031, Australia.

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had no history of epilepsy, serious illness, or operations; and was not taking any medications. Informed consent was obtained for the operative, anesthetic, and monitoring procedures, including manipulation of anesthetic dosages, in accordance with protocols approved by the Institutional Research Ethics Committee. Her preoperative hemoglobin concentration was 13.2 g/100 ml, Na<sup>+</sup>, 139 mmol/L; K<sup>+</sup>, 4.4 mmol/L; urea, 3 mmol/L; and creatinine, 0.06 mmol/L.

No premedication was given; anesthesia was induced with thiopentone, 200 mg, fentanyl, 100 µg, and pancuronium, 3 mg. Artificial ventilation with nitrous oxide and oxygen, 2:1, and sevoflurane was instituted using a tidal volume of 300 ml and a rate of 10 breath/min. The operation was performed with the patient in the prone position. The electrocardiogram, oxygen saturation, end-tidal carbon dioxide concentration, esophageal temperature, and intraarterial direct blood pressure were monitored. A warmed-air heating blanket was placed over the patient's lower body. Muscle relaxation was maintained with boluses of vecuronium so that there was no more than one twitch to train-of-four nerve stimulation of the ulnar nerve at the wrist. Mean blood pressure was maintained between 50 and 60 mmHg by varying the concentration of sevoflurane. End-tidal concentration of carbon dioxide remained between 35 and 40 mmHg, and body temperature decreased from 36.5 to 35.7°C during the procedure.

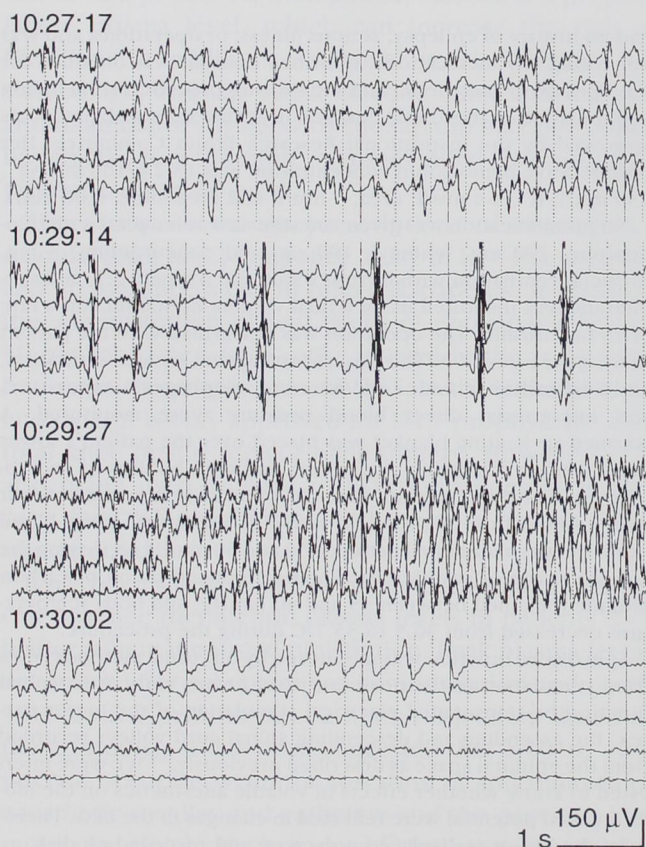
Spinal cord function was monitored by our usual methods: SEPs from stimulation of the posterior tibial nerves and corticospinal function by transcranial electrical stimulation of the motor cortex, the ascending and descending spinal cord volleys recorded from the epidural space as described previously.<sup>3,4</sup> We were interested to know whether effects of volatile anesthetics on the motor-evoked potential were reflected in changes in the EEG. Therefore, the EEG was displayed on screen and recorded on disk.

A 16-channel EEG was recorded continuously, using the International 10-20 System for electrode placement, on a digital EEG machine (DG Examiner, Medelec/Teca, Old Woking, Surrey, UK). It was inspected intermittently, and burst suppression was first noted to occur at a sevoflurane concentration of 4.5%.





**Fig. 1.** *Upper panel*, Selected channels of the EEG showing preconvulsive cerebral activity. *Lower panel*, Development of small spikes a short time later, using the same recording channels. Some of the spikes are highlighted by arrows.



**Fig. 2.** The two upper panels show further development of spike activity. The third panel shows the electroencephalographic seizure, and in the fourth, the seizure subsides, and the EEG becomes isoelectric. The five EEG channels are the same as in figure 1.

Operation time was 3 h, and blood loss was 2000 ml, replaced by 200 ml of autologous blood and two units of packed cells. Postoperative hemoglobin concentration was 10.2 g/100 ml. No movement by the patient was noted at any time during the operation, and she woke in the usual way at the end of the procedure. Postoperative recovery was slightly complicated by delayed return of bowel function, and total parenteral nutrition was administered from day 8 to day 11. The patient was discharged well, 12 days postoperatively.

The recorded EEG was replayed from disk, and hard copy was reviewed postoperatively. During the dissection phase of the operation and before any electrical stimulation was used for spinal cord monitoring, typical spike and polyspike seizure activity occurred for 30 s. The anesthesia record showed that at this time the inspired sevoflurane concentration had been 7% for 5 min, having been progressively increased from 2% over the previous 30 min. At approximately the time when the EEG seizure activity occurred, 50 µg of fentanyl was given, and the inspired concentration of sevoflurane reduced to 6%, where it remained for the next 40 min, subsequently being reduced over 35 min, adjusted to maintain blood pressure, and reaching zero at the time of wound closure. Oxygen saturation was 98%, end tidal carbon dioxide tension, 40 mmHg; and the blood pressure, 70/50 mmHg. There was no hemodynamic indication of a seizure; the pulse rate, which had been 120 beat/min for the previous 20 min, did not change during the seizure, but slowly decreased to 95 beat/min over the next 2.75 h, and the blood pressure was held constant by progressively decreasing the concentration of sevoflurane. The spike activity was followed by a period during which the EEG was isoelectric, followed by occasional spikes for the next 45 min. It is notable that transcranial electrical stimulation of the cortex produced no further seizure activity even under conditions favoring any such effect.

The figures illustrate selected EEG channels, showing pre-seizure cerebral activity (fig. 1, upper panel), the development of spike activity (Fig. 1, lower panel, and Fig. 2, upper panels), culminating in an EEG seizure (Fig. 2, third panel). After the



## CASE REPORTS

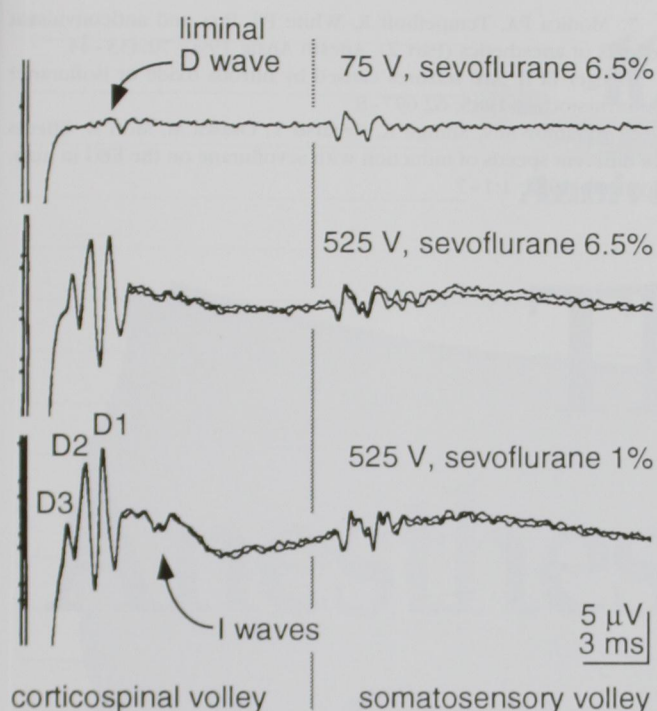


Fig. 3. Descending corticospinal volley evoked by electrical transcranial stimulation of the motor cortex (left of the dotted vertical line) and the ascending somatosensory volley evoked by simultaneous supramaximal stimulation of the tibial nerves in the popliteal fossae (right of the dotted line). In the upper panel, the transcranial stimulus was 75 V and produced a liminal D wave. In the middle panel, stimuli of 525 V produced a complex D wave volley with three components, but with little I wave activity (see references 3 and 4 for a more complete discussion of terminology). In the lowest panel, stimuli of the same intensity evoked a complex D wave with components of slightly larger amplitude, and with more clear I wave activity. Each trace is the average of 10 sweeps, with two consecutive averages superimposed in the middle and lowest panels.

seizure, the EEG was initially isoelectric, but spike activity then returned, subsiding as sevoflurane was withdrawn. It is of interest that sevoflurane, 7%, a concentration that produced spike and polyspike discharges in the EEG, had only minor depressant effects on the corticospinal volley set up by transcranial stimulation, attenuating I waves, and slightly decreasing the amplitude of the D wave components (Fig. 3) in a manner similar to isoflurane.<sup>5</sup>

## Discussion

To establish that an anesthetic agent is epileptogenic is complex.<sup>6,7</sup> Nitrous oxide is generally considered not to be epileptogenic, although the possibility has been raised,<sup>8</sup> based on a seizure occurring during induction. In this instance, it was postulated

that nitrous oxide may be epileptogenic, but the presence of other anesthetic agents would tend to oppose this action.<sup>8</sup> In the present report, a possible role for nitrous oxide in producing the seizure remains speculative.

Although 50  $\mu$ g of fentanyl was given at about the time of the seizure, this is unlikely to have caused epileptiform activity in the EEG. Fentanyl in low-to-moderate doses has not been associated with EEG evidence of seizures, nor has it been shown to have anticonvulsant effects in humans or animals.<sup>6</sup> This is the only patient in whom we have recorded the EEG during deep sevoflurane anesthesia, and hence the incidence of such changes is unknown.

In cats, sevoflurane suppresses background EEG activity, but it increases the EEG and SEP responses to high frequency stimuli to the skin or brain stem. These neurophysiologic properties are similar to those of enflurane, and hence it is possible that sevoflurane, like enflurane, may have convulsant properties.<sup>1</sup> During induction of anesthesia in humans with sevoflurane in oxygen, 10- to 14-Hz waves develop and increase in amplitude when the concentration is increased to 4% over 20 min, a pattern which is not seen with other volatile agents. In addition, during rapid induction with 4% sevoflurane in oxygen, high-amplitude rhythmic 2- to 3-Hz slow waves, which may represent CNS stimulation during anesthesia, have been reported.<sup>9</sup>

In summary, continuous spike and polyspike seizure activity occurred during EEG monitoring of a patient anesthetized with a high concentration of sevoflurane accompanied by nitrous oxide and low-dose fentanyl. The seizure discharge lasted 30 s. There were no post-operative sequelae.

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## CASE REPORTS

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