Comparison of the effects of sevoflurane and propofol on cortical somatosensory evoked potentials

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Background. Propofol (P) and sevoflurane (S) are potential anaesthetic agents if electrophysiological monitoring is required during spinal surgery. They allow rapid recovery and do not depress cortical somatosensory evoked potentials (SSEP) as much as other agents. The effects of these agents on SSEP have not been compared before.

Methods. Twenty-four patients were allocated randomly to receive either S (n=12) or P (n=12). SSEP evoked by electrical stimulation of the posterior tibial nerve at the ankle were recorded before anaesthesia. The cortical potential P40 was recorded (latency P40 and amplitudes N29P40 and P40N50). The anaesthetic concentration was adjusted gradually to obtain three predetermined ranges of values of bispectral index (BIS): 45–55, 35–45 and 25–35. For each range, a stable state was maintained for 10 min and SSEP were recorded.

Results. For the BIS 45–55 range, compared with preoperative values, P40 latency increased during S [mean change +2 (SD 0.6) ms] but not during P [+0.4 (0.2) ms (P= 0.12)] and both amplitudes (N29P40 and P40N50) decreased with S. Increasing S concentration caused a dose-dependent depression of SSEP. P did not have a statistically significant effect on the recordings and the signals remained stable in each BIS range.

Conclusion. Sevoflurane affected SSEP recordings in a dose-dependent fashion. Propofol had a minimal effect on SSEP recordings.

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Somatosensory evoked potentials (SSEP) are often used during spinal surgery to detect intra-operative spinal cord injury, but SSEP are sensitive to anaesthetics agents.1 2 In some studies the effects of anaesthetics interfered with SSEP recording. The relative effects of i.v. and inhaled agents on SSEP remain unclear because anaesthetic depth was not standardized. Auditory evoked potentials and the bispectral index (BIS) are both electrophysiological variables used to assess anaesthetic depth. The BIS uses electroencephalogram recording and is easier to acquire and analyse. It has been studied widely and is in routine use as a monitor.3–5 Because of short onset and recovery, propofol and sevoflurane are possible agents for spinal surgery that allow neurological examination soon after surgery.6 We compared anaesthesia using sevoflurane and propofol, measuring SSEP at different predetermined BIS values.

Patients and methods

Patients

After institutional review board approval (CCPPRB, Nice) and with written informed consent from each patient, we studied healthy adults about to have elective shoulder surgery. Inclusion criteria were American Society of Anesthesiologists physical status 1 or 2, age between 18 and 65 yr, normal findings on clinical neurological
examination and no history of nerve disease. The patients were allocated to one of two groups the day before surgery by the use of computer-generated random numbers.

Study plan
Baseline SSEP and BIS (BIS Monitor A-2000; Aspect Medical Systems, Natick, MA, USA) were recorded before anaesthesia as described below. Anaesthesia was obtained with intravenous propofol or inhaled sevoflurane according to allocation. After induction of anaesthesia, tracheal intubation was facilitated with atracurium 0.5–0.6 mg kg$^{-1}$ and was done 1 min after giving remifentanil 0.5 μg kg$^{-1}$. Volume-controlled ventilation of the lungs was started with a tidal volume of 7±10 ml kg$^{-1}$ using 50% oxygen in air and was adjusted by 0.5

$\text{F}_{\text{res}}$.

Volume-controlled ventilation of the lungs was started with a tidal volume of 7–10 ml kg$^{-1}$ using 50% oxygen in air and was adjusted to maintain end-tidal carbon dioxide in the 35–40 mm Hg range. Anaesthetic administration was adjusted to keep BIS values between 45 and 55 until there was less than 10% variation in BIS and less than 20% variation in mean arterial pressure (MAP) over a 10 min period of observation. SSEP evoked by stimulation of the posterior tibial nerve were then recorded. Two other recordings were made under the same conditions but with BIS held between 35 and 45 and between 25 and 35 for 10 min by gradually increasing the amount of the anaesthetic agent administered.

In the propofol group, anaesthesia was induced with a target-controlled infusion device (Master TCI-Diprifusor; Fresenius, Brezins, France). A target concentration of 4 μg ml$^{-1}$ was set to allow intubation. Then the infusion was reduced to a target concentration of 2 μg ml$^{-1}$ and adjusted by 0.5 μg ml$^{-1}$ increments in order to reach the three desired ranges of BIS values. In the sevoflurane group, anaesthesia was induced by inhalation of a gas mixture of 8% sevoflurane in 100% oxygen to vital capacity. Inspired and end-tidal (E $\text{T}$) concentrations of the anaesthetic agent, oxygen and carbon dioxide were measured. When E $\text{T}$ sevoflurane was 2 minimum alveolar concentration (MAC), the patient was intubated. Then the vaporizer (Vapor 19.5 vaporizers; Dräger, Lübeck, Germany) was adjusted until end-tidal concentration became 0.5 MAC and adjusted by steps of 0.2 end-tidal concentration to reach the three predetermined BIS ranges. Neither opioids nor nitrous oxide were given during the recordings. Core body temperature was measured with an oesophageal temperature probe and maintained above 36°C throughout the study period using a warming blanket and an i.v. fluid warmer. Each patient was given Ringer lactate 500 ml before induction then an infusion of 500 ml h$^{-1}$. MAP was measured non-invasively and was allowed to decrease to a stable value. Ephedrine was given if MAP decreased by more than 50 mm Hg. We recorded oxygen saturation from a pulse oximeter and heart rate and blood pressure every 5 min. All measurements were made before surgery.

Acquisition of cortical somatosensory evoked potentials
All measurements were made by the same trained neurophysiologist, who used the same apparatus each time and did not know which anaesthetic technique was being used. Measurements were made with the patient supine. SSEP were elicited by stimulation of the right posterior tibial nerve at the ankle (the right side was chosen arbitrarily) using silver chloride electrodes filled with conductive paste and placed 3 cm apart. Regular pulses of 20 mA lasting 0.5 ms were delivered at a rate of 3.1 Hz. Evoked potentials were recorded through subdermal needle electrodes placed over the cortex: the active electrode was placed on the scalp at C$z$, in the midline 2 cm behind the vertex C$z$ with a reference electrode placed 7 cm in front of C$z$. The ground electrode was placed on an arm. Recording electrode impedance was maintained at less than 3 kΩ. The amplifier band pass was 20 Hz to 2 kHz. An analysis time of 100 ms was used for each SSEP waveform and 125 sweeps were averaged. Stimulations and recordings were performed with a Compass Portabook (Nicolet Biomedical, Madison, WI, USA). Four sets of averages were checked for reproducibility and a grand average of 500 repetitions was produced from these four averages. Signal latency amplitude was determined with cursors by a masked observer. The latencies of P40 and amplitudes of N29–P40 and P40–N50 were noted.

Statistical analysis
Comparison of two means was with one-way analysis of variance and of several means with repeated measures analysis of variance. The relationship between the values of each parameter (latency and amplitudes) and the values of BIS was studied by linear regression analysis. For each subject, the Pearson linear coefficient was computed and tested for difference from zero. Data are presented as mean (SD). A P value less than 0.05 was considered to be statistically significant.

Results
Twenty-nine patients were eligible for this study. Two patients did not give informed consent and three patients were excluded after entry into the study because of poor or absent waveforms before anaesthesia (clinical history of low back pain: two in the P group and one in the S group). Therefore, the results from 24 patients were analysed. Table 1 shows patient details. Groups were similar in gender (six women and six men in each group) and there were no differences between the two groups. There were also no differences in temperature or blood pressure between the groups for the different recording periods. No ephedrine was required. The amounts of anaesthetic needed to obtain the BIS ranges of 45–55, 35–45 and 25–35 were predicted...
cortical SSEP to be monitored satisfactorily, and no differences were seen between the different groups and times of the study. Anaesthetic agents should have little or no effect on the signals if this form of monitoring is to be helpful. Opioids cause minimal change in the SSEP. Their effects appear to be related to drug concentration and maximal changes occur at concentration peak, after bolus delivery. Remifentanil was chosen for induction to reduce stimulation from laryngoscopy and intubation. A single injection of remifentanil is unlikely to affect the recordings because it has a short duration of action and rapid clearance. Recovery is delayed after midazolam.

Volatile agents can attenuate SSEP. Changes have been found at low concentrations, e.g. 0.5–1% expired concentration of isoflurane. Isoflurane reduces amplitude and increases latency in a dose-dependent manner. The effects on evoked potentials differ among the volatile agents. Some studies have shown that sevoflurane causes less depression than other volatile agents, allowing safe and reliable monitoring. Sevoflurane, like propofol, has rapid onset and recovery but our study shows that this agent, like other volatile anaesthetics, causes a dose-related increase in latency and decrease in amplitudes. Moreover, in two patients we noted total suppression of SSEP, which could cause a false alarm during spinal surgery.

Propofol allows rapid recovery and minimal post-operative confusion after major spinal surgery. We found that SSEP amplitudes did not change with propofol anaesthesia. Knowledge of the effects of propofol on the SSEP is limited. In some studies, propofol attenuated SSEP but it was usually administered as boluses given manually for induction and maintenance, which could have caused large variation in concentration. In the present study, we gave propofol using a target-controlled infusion technique. A stable predicted concentration was programmed to prevent overdosage and large changes in spinal and cerebral concentrations. In addition, most of the earlier studies were conducted with nitrous oxide, which is a potent depressant agent.

We confirmed previous findings, but these studies tested the effects of anaesthetic agents in different conditions: median nerve SSEP, animal studies, motor evoked potentials or subcortical SSEP. No comparison between i.v. anaesthesia and volatile anaesthetic agents was available. Our study is clinically relevant to scoliosis surgery because we compared the two agents using lower-limb cortical SSEP in humans. Cortical SSEP provide larger waveforms than subcortical SSEP and it is therefore easier to analyse them and to detect any changes. However, our study is limited because it was not performed during spinal surgery. The prone position can impair the SSEP by possible traction on lower spinal nerves. Secondly, the depth of anaesthesia assessed by BIS changes is affected by surgical stimulation. Therefore, the anaesthetic concentrations we report should not be taken as a target for use during surgery. Other studies provide further reasons for using propofol for SSEP

### Discussion

Cortical SSEP are a valuable measure of the function of the spinal cord during scoliosis surgery. Latency and amplitudes change with spinal cord injury. SSEP are also specifically depressed by deep anaesthesia. Clinical signs are unreliable for assessment of the depth of anaesthesia. The BIS has been proposed as a way of measuring the hypnotic effect of drugs and may be used to detect overdosage. Adequate hypnosis is achieved when the BIS value is between 45 and 55. Our study shows that, within this interval, sevoflurane depresses the SSEP while propofol does not change it significantly.

Factors such as body temperature and hypotension can affect the SSEP. We kept these factors stable to enable the

### Table 1 Patient characteristics and clinical details. Values are mean (SD or range)

<table>
<thead>
<tr>
<th></th>
<th>Propofol (n=12)</th>
<th>Sevoflurane (n=12)</th>
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<tbody>
<tr>
<td>Age (yr)</td>
<td>53 (31–67)</td>
<td>51 (26–69)</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>67 (8)</td>
<td>71 (10)</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>168 (8)</td>
<td>171 (7)</td>
</tr>
<tr>
<td>Core temperature (°C)</td>
<td></td>
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<tr>
<td>Baseline</td>
<td>36.5 (0.2)</td>
<td>36.4 (0.2)</td>
</tr>
<tr>
<td>BIS range 45–55</td>
<td>36.3 (0.4)</td>
<td>36.2 (0.3)</td>
</tr>
<tr>
<td>BIS range 35–45</td>
<td>36.1 (0.3)</td>
<td>36.1 (0.3)</td>
</tr>
<tr>
<td>BIS range 25–35</td>
<td>35.9 (0.4)</td>
<td>35.8 (0.5)</td>
</tr>
<tr>
<td>Mean arterial pressure</td>
<td>91 (17)</td>
<td>94 (13)</td>
</tr>
<tr>
<td>Baseline recording (mm Hg)</td>
<td>89 (15)</td>
<td>88 (10)</td>
</tr>
<tr>
<td>BIS range 45–55</td>
<td>86 (14)</td>
<td>81 (7)</td>
</tr>
<tr>
<td>BIS range 35–45</td>
<td>84 (10)</td>
<td>80 (8)</td>
</tr>
<tr>
<td>BIS range 25–35</td>
<td>78 (10)</td>
<td>79 (8)</td>
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Concentrations of 2.3 (0.3), 3.4 (0.4) and 5.2 (0.5) μg ml⁻¹ respectively for propofol and 0.5 (0.2), 0.9 (0.3) and 1.3 (0.3) MAC for sevoflurane. The mean BIS values for the three ranges were 52 (2), 41 (3) and 29 (2) respectively for propofol and 53 (3), 39 (2) and 31 (3) for sevoflurane. There were no differences between ranges of BIS values for either of the two agents.

Before anaesthesia, comparisons of latencies and amplitudes showed no difference between groups. Baseline SSEP showed wide intersubject variability in peak-to-peak amplitudes. With sevoflurane, the correlation with BIS range was statistically significant: it was positive for latency and negative for amplitude (Fig. 1). When the BIS target range of 45–55 was achieved, latency P40 increased compared with the control value (Table 2). For both amplitudes, signals also decreased compared with the control value. SSEP waveforms were totally suppressed in two patients (one at 35–45 and one at 25–35 BIS). With propofol, no correlation was found. When the BIS target range of 45–55 was achieved, latency P40 remained stable compared with the control value, as did both amplitudes. Propofol did not suppress SSEP at any BIS range.

\[ \text{Mean arterial pressure} = \text{Baseline recording} + \text{BIS range} + \text{Baseline} \]

\[ \text{Age (yr)} = \text{53 (31–67)} \]

\[ \text{Weight (kg)} = \text{67 (8)} \]

\[ \text{Height (cm)} = \text{168 (8)} \]

### Factors such as body temperature and hypotension can affect the SSEP. We kept these factors stable to enable the

### Discussion

Cortical SSEP are a valuable measure of the function of the spinal cord during scoliosis surgery. Latency and amplitudes change with spinal cord injury. SSEP are also specifically depressed by deep anaesthesia. Clinical signs are unreliable for assessment of the depth of anaesthesia. The BIS has been proposed as a way of measuring the hypnotic effect of drugs and may be used to detect overdosage. Adequate hypnosis is achieved when the BIS value is between 45 and 55. Our study shows that, within this interval, sevoflurane depresses the SSEP while propofol does not change it significantly.

Factors such as body temperature and hypotension can affect the SSEP. We kept these factors stable to enable the
recording, with stable waveforms after prolonged administration. For inhaled agents, accumulation can affect recordings.

Hypnotic actions suppress inter neuronal activity. Anaesthetic effects are more pronounced in cortical SSEP than in subcortical SSEP because of the large number of cortical synapses. The longer latency under sevoflurane compared with baseline values and propofol infusion suggests that volatile agents affect these synaptic transmissions. In an experimental study, Wakasugi and colleagues showed that volatile agents increase inhibitory activity [gamma-aminobutyric acid (GABA)] and decrease excitatory activity [N-methyl-D-aspartate (NMDA)]. Intravenous drugs might act only on GABA receptors, not on NMDA receptors. This would explain the less depressive effect of propofol than of sevoflurane on SSEP.

Fig 1 Scatter diagrams of linear regression relationship between BIS values and SSEP features.

<table>
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<th>Table 2</th>
<th>Changes in SSEP before and during sevoflurane and propofol administration at BIS range 45–55. There were 12 subjects in each group. Values are mean (SD). Before anaesthesia, comparisons of latencies and amplitudes showed no difference between groups. *P&lt;0.05 vs control; †P&lt;0.05 vs propofol</th>
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<tr>
<td></td>
<td>Control</td>
</tr>
<tr>
<td>P40 latency (ms)</td>
<td>Sevoflurane: 39.9 (3.9)</td>
</tr>
<tr>
<td></td>
<td>Propofol: 38.8 (3.3)</td>
</tr>
<tr>
<td>N29-P40 amplitude (μV)</td>
<td>Sevoflurane: 1.38 (0.89)</td>
</tr>
<tr>
<td></td>
<td>Propofol: 1.25 (0.4)</td>
</tr>
<tr>
<td>P40-N50 amplitude (μV)</td>
<td>Sevoflurane: 2.36 (1.30)</td>
</tr>
<tr>
<td></td>
<td>Propofol: 2.27 (1)</td>
</tr>
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</table>
In summary, sevoflurane has effects on SSEP that are
typical of other volatile agents when the concentration is
gradually increased. At a proper depth of anaesthesia,
sevoflurane altered SSEP and propofol did not. Moreover,
the signal can be totally suppressed if the BIS is less than 45.
Therefore, sevoflurane will affect the monitoring of the
spinal cord even if the level of hypnosis is carefully
controlled, and propofol is a more suitable agent.

Acknowledgement
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