Effects of Isoflurane and Desflurane on Neurogenic Motor- and Somatosensory-evoked Potential Monitoring for Scoliosis Surgery

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Background: Most techniques used to monitor spinal cord tracts are sensitive to the effects of anesthesia, particularly to volatile anesthetic agents. The aim of this prospective study was to show that evoked potentials recorded from the peripheral nerves after spinal cord stimulation, so-called neurogenic motor evoked potentials, are resistant to clinical concentrations of isoflurane or desflurane, compared with somatosensory-evoked potentials.

Methods: Twenty-three patients were studied during surgery to correct scoliosis. The background anesthetic consisted of a continuous infusion of propofol. Isoflurane (n = 12) or desflurane (n = 11) were then introduced to achieve 0.5 and 1.0 end-tidal minimum alveolar concentrations (MAC), both in 50% oxygen–nitrous oxide and in 100% oxygen. Somatosensory-evoked potentials were elicited and recorded using a standard method, defining cortical P40 and subcortical P29. Neurogenic motor-evoked potentials were elicited by electric stimulation of the spinal cord via needle electrodes placed by the surgeon in the rostral part of the surgical field. Responses were recorded from needle electrodes inserted in the right and left popliteal spaces close to the sciatic nerve. Stimulus intensity was adjusted to produce a supramaximal response; that is, an unchanged response in amplitude with subsequent increases in stimulus intensity. Measurements were obtained before introducing volatile agents and 20 min after obtaining a stable level of each concentration.

Results: Isoflurane and desflurane in both 50% oxygen–nitrous oxide and 100% oxygen were associated with a significant decrease in the amplitude and an increase in the latency of the cortical P40, whereas subcortical P29 latency did not vary significantly. Typical neurogenic motor-evoked potentials were obtained in all patients without volatile anesthetic agents, consisting of a biphasic wave, occurring 15 to 18 ms after stimulation, with an amplitude ranging from 1.3 to 4.1 µV. Latency or peak-to-peak amplitude of this wave was not significantly altered with isoflurane and desflurane, either in the presence or in the absence of nitrous oxide.

Conclusions: Compared with cortical somatosensory-evoked potentials, neurogenic motor-evoked potential signals are well preserved in patients undergoing surgery to correct scoliosis under general anesthesia supplemented with isoflurane or desflurane in concentrations as great as 1 MAC. (Key words: Anesthetics, volatile; isoflurane, desflurane. Spinal cord. Somatosensory-evoked potentials; motor-evoked potentials.)

ALTHOUGH somatosensory-evoked potentials (SSEPs) during surgery to correct spinal deformities have been established as a standard for electrophysiologic intraoperative monitoring of the spinal cord, 1 the risk of damage to the motor tracts in the presence of unaltered SSEPs persists. 2 3 To ensure the functional integrity of the spinal cord during surgery, some authorities thus recommend that a “wake up” test be performed or that motor-evoked potentials (MEPs) be monitored in combination with SSEPs. However, most procedures eliciting intraoperative MEPs are highly sensitive to anesthesia, particularly volatile anesthetic agents. 4 5 6 7 8 9 so that it is difficult to monitor muscle MEPs elicited by transcranial stimulation even if low concentrations of these anesthetics are administered. 10 Muscle relaxants also greatly reduce the MEP recorded from muscle, 10 although interpretation is still compatible with a constant level of controlled neuromuscular blockade. 11 12

In 1988, Owen and colleagues 8 9 described a method for recording responses from the peripheral nerves after electric stimulation of the spinal cord (so-called neurogenic motor-evoked potentials [NMEPs]), primarily motor in origin but also containing an antidromic component. This method proved to be sensitive and reliable in many experimental and clinical reports. 11 13 In addition, NMEPs allow the use of muscle relaxants during surgery.
because a neurogenic, rather than myogenic, potential is recorded.

No prospective controlled human study has compared the effects of volatile anesthetics on NMEPs and SSEPs during extensive spinal surgery. Our goal was to test the hypothesis that NMEPs could be preserved during surgery to correct scoliosis with an anesthetic technique supplemented by low concentrations of isoflurane and desflurane.

Materials and Methods

This study was approved by our institutional review board and informed consent was obtained from each patient or their parents or guardians. Twenty-three consecutive adolescents or adults undergoing posterior spinal fusion (Cotrel-Dubousset instrumentation) to correct idiopathic scoliosis were studied. All patients had normal results of electrophysiologic examinations at the preoperative visit, including SSEPs, nerve conduction study, and motor potentials evoked by transcranial magnetic stimulation, using standard techniques. Oral premedication with 5 mg midazolam was given 60 min before induction of anesthesia, which was accomplished with 3 mg/kg propofol, 1 µg/kg sufentanil, and 0.1 mg/kg vecuronium to facilitate endotracheal intubation and prone positioning. Anesthesia was maintained using a continuous infusion of 4 or 5 mg·kg⁻¹·h⁻¹ propofol and 50% nitrous oxide in oxygen. A second injection of vecuronium (0.025 to 0.030 mg/kg) was given at the incision to facilitate surgical exposure. Because the compound muscle action potential can interfere with NMEP recording, supplemental vecuronium was therefore administered at the specific request of the neurophysiologist to suppress muscular artifacts from the NMEP recordings. Lungs were mechanically ventilated using an open circuit and a fresh gas flow of 6 to 8 L/min. Ventilation was adjusted to maintain end-tidal carbon dioxide between 32 and 35 mmHg. Monitoring included electrocardiograms, pulse oximetry, and capnography; and direct arterial pressure, central vascular pressures, and core temperature were measured.

Somatosensory-evoked potentials were elicited by bilateral stimulation of the posterior tibial nerves at the ankle using subdermal needle electrodes. Rectangular pulses lasting 0.2 ms were presented at a rate of 2.8 Hz. Evoked potentials were recorded through needle electrodes placed over the cortex, defining two channels: Cz active electrode, in the midline of the scalp 2 cm behind Cz, referenced to a midfrontal (Fpz) electrode, recording cortical P10, and Cz referenced to the earlobe, recording subcortical P29. The amplifier bandpass was 2 Hz to 3 KHz. An analysis time of 100 ms was used; for each SEP waveform, 300 to 1000 sweeps were averaged. Latencies of P29 and P40 and peak-to-peak amplitude of P40 were determined. A first set of SEP recordings was obtained before the second injection of vecuronium; approximately 45 min after induction. Stimulus intensity was adjusted above the motor threshold and was maintained at this level during surgery.

Neurogenic MEPs were obtained by stimulating the spinal cord through sterile platinum needle electrodes inserted by the surgeons above the surgical field either into the cancellous bone of the spinous processes the tips of which were resected or into the epidual space, depending on surgical access. The cathode was inserted into the vertebrae closest to the operating field, and the anode was placed into the next rostral one. An electric stimulus delivered rectangular pulses lasting 1 ms at a rate of 0.9 Hz. Stimulus intensity was adjusted to produce a supramaximal response (i.e., a response that did not increase further in amplitude with subsequent increases in stimulus intensity, usually 25 to 50 mA, and was unchanged during the surgery). Bilateral recording needle electrodes were inserted close to the sciatic nerve in the popliteal space. Filters were set at 30 and 3,000 Hz and analysis time was 50 ms. For each NMEP waveform, 10 to 20 sweeps were averaged, and onset latency (the time from stimulus to the first negative deflection) and peak-to-peak amplitude of the initial NMEP complex were determined. A first set of NMEPs was obtained approximately 90 min after the incision, this time being required for subperiosteal stripping of soft tissues and electrode insertion.

Evoked potentials were recorded and analyzed using a Nicolet Viking II (Nicolet, Madison, WI) machine. The wave forms were stored on magnetic disks for further retrieval.

Isoflurane or desflurane were introduced through a calibrated vaporizer. The first 12 patients received 0.6% and 1.3% end-tidal concentrations of isoflurane and the others received 3.7% and 7.4% end-tidal concentrations of desflurane (i.e., concentrations approximately equal to 0.5 and 1.0 MAC, respectively). For both agents, anesthetic concentrations were administered in an increasing order and monitored using a calibrated Datex capnomac Ultima anesthetic monitor (Datex, Helsinki, Finland). Somatosensory-evoked potentials and NMEPs were obtained before introducing volatile agents and 20 min after.
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obtaining a stable level of each end-tidal concentration. At each time, data were obtained in 50% oxygen - nitrous oxide, and then after 5 to 10 min of 100% oxygen inhalation. All measurements were recorded in duplicate for each patient before the rods of the surgical instrumentation were inserted. Because hemodynamic instability may result from specific surgical maneuvers of the spine, no measurements were performed during application of selective distraction on the vertebrae by the surgeons. Higher concentrations of volatile anesthetic agents were not tested to avoid excessive decreases in blood pressure.

For each volatile anesthetic agent, comparisons of latencies and amplitudes of potentials were made using a two-way analysis of variance for repeated measurements where the two factors were treatments (oxygen or nitrous oxide) and concentrations (before and at 0.5 and 1.0 MAC). After a significant F statistic, multiple comparisons within and between groups were performed using Student's t tests followed by Bonferroni corrections. Analysis included all the left recordings and all the right recordings, separately. Left- and right-side recordings were compared using an analysis of variance. A probability value less than 0.05 was considered significant. Descriptive statistics are expressed as mean ± SD.

Results

Table 1 contains demographics and intraoperative characteristics. Baseline data were obtained after 151

Table 2. Changes in Somatosensory Evoked Potentials before and during Isoflurane Administration in 50% Nitrous Oxide and 100% Oxygen

<table>
<thead>
<tr>
<th>Potentials</th>
<th>Before Isoflurane</th>
<th>0.6 vol % Isoflurane</th>
<th>1.3 vol % Isoflurane</th>
</tr>
</thead>
<tbody>
<tr>
<td>P29 latency (ms)</td>
<td>50% O₂-N₂O</td>
<td>31.3 ± 2.0</td>
<td>31.6 ± 2.4</td>
</tr>
<tr>
<td></td>
<td>100% O₂</td>
<td>31.0 ± 2.4</td>
<td>31.5 ± 3.5</td>
</tr>
<tr>
<td>P40 latency (ms)</td>
<td>50% O₂-N₂O</td>
<td>41.4 ± 2.7</td>
<td>43.0 ± 3.5*</td>
</tr>
<tr>
<td></td>
<td>100% O₂</td>
<td>41.4 ± 2.7</td>
<td>42.9 ± 2.7*</td>
</tr>
<tr>
<td>P40 amplitude (µV)</td>
<td>50% O₂-N₂O</td>
<td>1.2 ± 1.0</td>
<td>0.8 ± 0.7*</td>
</tr>
<tr>
<td></td>
<td>100% O₂</td>
<td>2.0 ± 1.4</td>
<td>1.3 ± 1.0*</td>
</tr>
</tbody>
</table>

Values are mean ± SD (n = 12 subjects). No significant differences were found between each mixture (50% O₂-N₂O vs. 100% O₂).

†P < 0.05 versus Before Isoflurane.
*P < 0.05 versus 0.6 vol % Isoflurane.

± 22 min of propofol infusion in the isoflurane group and 13 ± 27 min of propofol infusion in the desflurane group. Core temperature decreased slowly in both groups (one-way analysis of variance; P < 0.01). Significant hypotension resulted from increasing concentrations of isoflurane (one-way analysis of variance; P < 0.001) or desflurane (one-way analysis of variance; P < 0.001) (table 1). There was no suspicion of intraoperative neurologic complications. After recovering from anesthesia, results of neurologic examinations were normal in each patient.

Isoflurane and desflurane administration in both 50% oxygen - nitrous oxide and 100% oxygen was associated with a decrease in the amplitude and an increase in the latency of the cortical P40. For both agents, subcortical P29 latency did not vary significantly. No statistical significance was achieved for a greater depression of the signals in the presence than in the absence of nitrous oxide (tables 2 and 3).

Reproducible NMEPs were recorded from bilateral sciatic nerves in all patients immediately after the surgeries had inserted electrodes at the upper extremity of the operating field. Neurogenic MEP recording consisted of a large and mainly biphasic wave, 15 to 18 ms after stimulation. There was a wide intersubject variability in the peak-to-peak amplitude, ranging from 1.3 to 4.1 µV for the initial wave. All patients received one or more injections of vecuronium to eliminate muscular contamination of the NMEPs (mean dosage: 9.6 mg, including induction dose and the second injection; range, 6 to 14 mg). Neurogenic MEPs were maintained throughout the

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administration of isoflurane or desflurane without any significant changes in amplitude or in latency in both 100% oxygen and 50% oxygen–nitrous oxide (tables 4 and 5). Figure 1 illustrates typical recordings of SSEPs and NMEPs during isoflurane administration. No differences were observed between left and right recordings. Results of the right side were chosen arbitrarily for tables.

Discussion

This study shows that concentrations of isoflurane and desflurane, approximately 0.5 and 1.0 MAC, do not interfere significantly with intraoperative recording of MEPs, provided that these signals are recorded from peripheral motor nerves after electric stimulation of the spinal cord according to the method described by Owen and associates.13 These results in humans are consistent with those reported in rats by Russell and coworkers,22 who used a similar technique and found no differences in NMEPs between awake status and deep anesthesia induced by isoflurane in sufficient concentration to produce isoelectricity on the electroencephalogram. Except for possible variations due to species,23 it appears therefore that isoflurane and desflurane are compatible with NMEP recording and monitoring, which contrasts with most other techniques of intraoperative MEP monitoring.1-9

Previous studies have found marked anesthetic-induced changes in MEP recordings. Volatile anesthetic agents,1-8 as well as nitrous oxide,9 barbiturates,10 propofol, etomidate, and midazolam11-13 can alter MEPs recorded from muscles after transcranial magnetic or electric stimulations. Other approaches consist of electrically stimulating the cortex and recording the activity of a corticospinal tract synapse-free segment from electrodes placed in the epidural space of the spinal cord. Despite the possibility of some depressant effects, even on components that appear to be generated by direct stimulation of corticospinal axons,21,25 no difficulty is encountered in clinical practice for recording D-wave activity in patients under volatile anesthetic agents with this method.26,27 However, below the T10/T11 level, epidural recording might be problematic because that area contains a small number of corticospinal tract axons and because the evoked potential amplitude becomes too small to allow reliable monitoring.20 Because surgical instrumentation of scoliosis correction and other major spine surgeries nearly always include lower

| Table 3. Changes in Somatosensory Evoked Potentials before and during Desflurane Administration in 50% Nitrous Oxide and 100% Oxygen |
|-----------------|----------------|----------------|
| Before          | 3.7 vol % Desflurane | 7.4 vol % Desflurane |
| P29 latency (ms) | 30.8 ± 2.6          | 30.9 ± 2.6       |
| 50% O2–N2O      | 30.2 ± 1.7          | 30.5 ± 1.7       |
| 100% O2         | 30.8 ± 1.7          | 30.5 ± 1.7       |
| 100% O2        | 30.8 ± 1.7          | 30.5 ± 1.7       |
| P40 latency (ms) | 40.3 ± 4.3          | 41.6 ± 4.0       |
| 50% O2–N2O      | 39.8 ± 5.0          | 41.6 ± 4.0       |
| 100% O2         | 39.9 ± 5.0          | 41.7 ± 4.0       |
| P40 amplitude (µV) | 12 ± 1.3            | 11 ± 1.3         |
| 50% O2–N2O      | 12 ± 1.3            | 11 ± 1.3         |
| 100% O2         | 12 ± 1.3            | 11 ± 1.3         |

Values are mean ± SD (n = 11 subjects). No significant differences were found between each mixture (50% O2–N2O vs. 100% O2).

*P < 0.05 versus Desflurane.
†P < 0.05 versus 3.7 vol % Desflurane.

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anterolateral cortices,26-29 and it seems to be the norm, that the potential recordings are not affected by transectional lesions. NMEPs in the lower limbs suggests that the method of ventral function may be an excellent tool for monitoring motor nerves as well as for monitoring spinal nerves via sensory fibers within the spinal nerves. It is necessary to investigate whether anesthesia would prevent markers.20

Volatile anesthetic effects on the peripheral and spinal tracts remain a subject of concern, because the use of anesthetic would not appear to be beneficial.
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Fig. 1. Representative somatosensory-evoked potentials (right) and neurogenic motor-evoked potentials (left) in a 20-year-old patient during maintenance of anesthesia with propofol, before and during administration of isoflurane (0.6% and 1.3% end-tidal), in 100% oxygen. Duplicate waveforms are superimposed to show reproducibility.

![Diagram of NMEPs and SEPs](image)

from electrodes placed in the epidural space, and that NMEPs during administration of high-concentration isoflurane represent preferential preservation of antidromic sensory volleys over motor activity. However, despite the use of low concentrations of isoflurane or desflurane in the present study, the spinal stimulation frequently induced muscle contraction in the legs if neuromuscular blockade was inefficient. This finding attests to persistent anterior horn cell excitability and suggests that the NMEPs we recorded did contain motor tract activity. Because studies that have specifically looked at anesthetic effects on the spinal motor neuronal system have observed a remarkable sensitivity to isoflurane-induced depression, a shift in the relative contribution of the sensory and motor components of the NMEPs might occur during increasing anesthetic concentrations. Anesthetic-induced modifications of NMEP structure could argue for this assumption because the major biphasic wave of NMEPs is conducted mainly by the anterolateral motor tracts, and the polyphasic waves are generated in the dorsal spinocerebellar tracts and the dorsal columns. However, with the anesthetic concentrations we tested, we observed no significant change in wave structure.

A low-concentration of isoflurane in nitrous oxide, which with minor variations is among the most common anesthetic technique used in Europe and the United States, has been reported to induce substantial depression of cortical SEP waves yet is compatible with monitoring. We addressed no statistical comparisons between desflurane and isoflurane in the absence of a randomized design, but it is clear that desflurane

vertebral levels, the utility of epidural recording is thus limited.

Neurogenic MEPS appear to be composed of both anterolateral motor tracts and dorsal column activities, although the relative contribution of these pathways to the sciatic response is unclear. Data support the notion that a motor component is involved in these potentials, particularly when high-intensity stimulations are used, as in our study. Both the experimental transection of the anterior columns and the accidental lesions during spinal surgery show that loss of NMEPs is followed by postoperative paralysis of the lower limbs, even when SEPs are unchanged, which suggests that NMEPs could represent a convenient method for monitoring spinal cord function. On the other hand, it has been shown experimentally that responses recorded from peripheral nerves after spinal cord stimulation were at least partially dependent on antidromic activation of the sensory fibers tii the dorsal column. Involvement of the sensory component has also been established in humans using pure sensory nerve recordings and collision techniques. Thus an NMEP alteration does not necessarily reflect a motor lesion but can be the result of a dorsal column lesion.

Volatile anesthetics are responsible for depressive effects on motor transmission between the central and the peripheral nervous systems by acting on the corticospinal tract tii the alpha motoneuron synapse. Thus we could argue that the motor component of NMEPs would not be recorded during administration of such anesthetics, as opposed to the synapse-free recording

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leads to depressed SSEPs, so that similar conclusions could be drawn. As already shown by others,\textsuperscript{46,47} the subcortical SSEPs (i.e., the P29 waves that are not much affected by volatile anesthetics, as in our study) might be preferable to those of cortical origin for spinal cord monitoring. However, the main criterion used for monitoring purposes is the wave amplitude. Cortical SSEPs amplitude is markedly decreased by isoflurane and desflurane, and the reliability of the subcortical P29 amplitude in diagnosing spinal cord injury during surgery has not yet been studied.

Because of their dual origin, NMEPs could be helpful for providing concurrent data from both motor and sensory pathways. Neurogenic MEPs have been proved to be reliable signals to monitor the entire spinal cord activity,\textsuperscript{17}\textsuperscript{-18} although the sensory and motor components have different sensitivities to ischemia\textsuperscript{19} and possibly to anesthetic concentrations. Owen and colleagues\textsuperscript{7} reported a 5.6% false-negative rate, but no false-negative results, during spinal cord monitoring of 300 patients having orthopaedic, neurologic, or cardiothoracic surgery. Preliminary results found this technique promising during correction of scoliosis.\textsuperscript{10} It appears from our study that isoflurane and desflurane superimposed on a background of nitrous oxide and propofol anesthetic may be used for spinal procedures in which spinal cord function will be monitored, provided that NMEPs are recorded.

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