Effects of Desflurane on Conductive and Segmental Spinal Cord Evoked Potentials

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Abstract

Background and purpose
The object of this study was to investigate and compare the effects of the newest volatile anesthetic, desflurane, on the common intraoperative neuromonitoring models, conductive- SCEP elicited by spinal cord stimulation and segmental- SCEP by peripheral nerve stimulation.

Materials and methods
Ten adult Wistar rats were placed under general anesthesia by endotracheal intubation with mechanical ventilation, and close vital signs monitoring. Needle recording electrodes were placed stereotactically into T11/12 interspinous ligament; conductive-SCEP elicited by C2/3 interspinous stimulation, and segmental- SCEP by sciatic nerve and posterial tibial nerve stimulation were obtained. The effects of desflurane were examined at various end-tidal concentrations of 6, 9, and 12 %.

Results
The peak-to-peak amplitude and the latency of the major wave in all three kinds of potentials decreased and delayed gradually with higher concentration. Comparing 9 % with 6 % desflurane, the amplitude decreased to 86.8, 75.8, and 83.2 % in conductive-SCEP, sciatic nerve and posterial tibial nerve elicited segmental-SCEP respectively; there is no significant statistical difference by ANOVA. However, at 12 %, again compared with 6 %, the amplitude decreased further to 66.2, 26.4, 40.5 % respectively; the conductive SCEP preserved more than the segmental SCEPs significantly (p=0.04).
Conclusion

We concluded that the concentration of desflurane alters the amplitude of SCEPs, and to a lesser degree, delays the latency; and the segmental SCEPs are more liable to be suppressed by desflurane than the conductive SCEP. These findings indicate that the dose-dependent suppression effect on amplitude of desflurane should be considered when studying evoked potential effects during surgery. Furthermore, the potential benefit of conductive-SCEP in intraoperative neuromonitoring should be considered because of its higher resistance with greater concentration of desflurane.
Introduction

Somatosensory evoked potential (SSEP) monitoring is the very reliable and common use model of intraoperative neuromonitoring for observing the functional integrity of neural tissue in which there is a risk for brain, spinal cord or peripheral nerve injury. However, clinical practice and experimental researches of these techniques has shown that all kinds of evoked potentials are very sensitive to suppression by anesthetic agents, particularly volatile anesthetic agents. Desflurane, a newest derivative of isoflurane, had the most striking difference as the low solubility and more rapid cerebral washin and washout than other volatile anesthetics, which may play a role in the overcome of anesthetic-induced depression. However, Haghighi et al demonstrated that desflurane significantly altered the amplitude of transcortical motor evoked muscle potentials and cortical- and spinal- SSEPs. Although spinal SSEP was demonstrated to be more resistant than cortical SSEP, there was still over fifty percent reduction in amplitude at MAC level of 2, when the stimulation is delivered in the peripheral nerve indirectly (posterior tibial nerve). Considering the SSEP monitoring system has increasingly been carried out with spinal rather than cortical recording and there are several different stimulation techniques for monitoring spinal SSEP could be attempted and the effect of desflurane on these different potentials is unclear. Therefore, we evaluated the effect of desflurane on spinal SSEP elicited by electrical stimulation indirectly on the distal portion of posterior tibial nerve, and sciatic nerve, spinal cord directly in rats. The aims of the present study was to verify the effect of desflurane on the different models of spinal SSEPs, and to identify the most appropriate technique of stimulation in spinal SSEPs recording.
Material and method

Animal preparation and recording of evoked potential

Fifteen Wistar rats weighting 412 to 526 g were used for this study. Induction of the anesthesia was accomplished in a plexiglass box, using desflurane (9%) in 2 liters' oxygen for five minutes. Then a endotracheal tube (16 # intravenous catheter) was inserted by the method we reported before for controlled ventilation (tidal volume, 5ml/kg, rate, 40 breath/min), with an IPPB RESPIRATOR UR-100 (SHIN-EI INDUSTRY CO., LTD, Japan). An intravenous line from the right femoral vein was set up for fluid administration and another 22 gauge catheter was also cannulated into the ipsilateral femoral artery for continuous monitoring of heart rate and blood pressure (Datex, CARDIOCAP, CM-104-28-01). The blood gas samples were obtained intermittently (periodically, when every change of concentration of desflurane) from the arterial line too. A rectal thermometer was inserted, and body temperature was maintained at approximately 38 C with a warm water mattress and a heating lamp. The animals were turned prone and the head was fixed in a stereotactic frame. A 5-centimeter longitudinal incision was made in the back, from the T-L junction to the upper sacral spine. Spinal somatosensory evoked potential (SSEP) was recorded from a needle electrode inserted in the T-L junction interspinous ligament, and a reference electrode placed in subcutaneous tissue just proximal to the recording electrode. Three different kinds of spinal SSEPs as segmental SSEP elicited by direct sciatic nerve stimulation and indirect posterior tibial nerve, and conductive SSEP elicited by direct spinal cord stimulation were recorded by the following stimulation preparation. After dorsal incision of left thigh was used to expose a 1.5cm segment of sciatic nerves, stimulation of the left sciatic nerves was via two hook-needle electrodes (Nihon Koden, Tokyo, Japan) placed 5 mm apart adjacent to the sciatic nerve with the cathode being
proximal. Another pair needle electrodes were inserted into the paw near the plantar ending of posterior tibial nerve. A 2-centimeter longitudinal incision was made in the back of neck, from the base of the skull to the upper cervical spine, and stimulation of the cervical spinal cord was via two needle electrodes (Nihon Koden, Tokyo, Japan) placed 5 mm apart, inserted into the C2/3 interspinatous ligament with the cathode being proximal. Rectangular impulses of 0.2 milliseconds duration were presented at a rate of 5 Hz, and stimulus intensity was set at supramaxial level, i.e., four to five times greater than required to produce a visible twitch of the paw. A ground electrode placed in the pelvic girdle in the recording of sciatic nerve and posterior tibial nerve segmental SSEPs, and in the shoulder girdle in the recording of conductive SSEP. The potentials were averaged 20 times at a band-pass filter setting of 50 to 5000 Hz with a 20-millisecond time base. Desflurane was introduced at 6 % for fifteen minutes and the segmental and conductive SSEPs were recorded under this stable concentration. Meantime, the heart rate, blood pressure and blood gas analysis were measured. After the SSEPs recorded at 6 % desflurane as control, desflurane was administrated at an inspired concentration of 9 % and then of 12 %. After fifteen min of desflurane administration at each concentration, SSEPs in response to all three different stimulation modes were recorded. The change of the vital signs were also measured. At the end of each experiment, the animal was killed by an overdose injection of Pentothal. Amplitude was measured from the peak to the trough of the major wave within the evoked response. Latency of the response was measured from the onset of the electrical shock artifact to the initial positive peak. These peak latency and the peak-to-peak were measured and calculated at each concentration. To compare variable parameter of vital sign and amplitude and latency of SSEPs during the administration of desflurane, one way analysis of variance with repeated measures was used. Results are showed in mV in amplitude and ms in latency, and in relative percentage of 9 to 6 % and 12 to 6 %.
statistical results are considered significant at $P < 0.05$ and all data are expressed as mean ± SEM.
Result

Physiologic data are presented in table 1. Except the progressive, but non-significant reduction of systolic, diastolic and mean arterial pressure associated with the increase of the concentration; the data of PaO2, PaCO2, Arterial pH, and heart rate were similar among groups of different concentrations. In generally, the concentration of desflurane required to produce hypotension was 12 %.

Figure 1 shows representative recordings of the typical waveforms of three different potential and the effects of desflurane on these potentials. These responses typically show a initial small positive wave and a major negative wave.

The amplitude of indirect posterial tibial nerve stimulation elicited spinal-SSEP varied between 20.5 and 195 uV (average = 55.2 ± 32.5); the onset latency range from 3.16 to 5.28 ms (average = 3.88 ± 0.53) in 6% desflurane. The data were 65 to 275 uV (average = 166.9 ± 62.3) and 15 and 180 uV (average = 166.4 ± 122.4) of direct sciatic nerve and spinal cord stimulation elicited spinal-SSEP in amplitude, and there were significant larger amplitude than the indirect posterial tibial nerve stimulation elicited spinal-SSEP. In latency, the data were were1.2 to 1.84 ms (average = 1.51 ± 0.17) and 1.04 and 2.44 ms (average = 1.60 ± 0.36) of direct sciatic nerve and spinal cord stimulation elicited spinal-SSEP in amplitude, and the significant shorter latency than the indirect posterial tibial nerve stimulation elicited spinal-SSEP was due to the conduction distance. Table 2 and 3 summarized the difference in amplitude and latency in the different spinal SSEP in different desflurane concentrations.

Fig 1 also shows representative potentials changes during the administration of 6, 9 and 12 % desflurane. During the administration of 6 and 9 % desflurane, the spinal-SSEPs could be recorded in all animal (15/15) by direct sciatic nerve or indirect PT nerve stimulation, and in 11 animals (73.3 %) by spinal cord stimulation. There is statistical
significance (p=0.02). In the administration of 12 % desflurane, the percentage of positive recording change to 15 rats (100 %), 12 rats (80 %), and 9 rats (60%) of sciatic, PT, and spinal cord stimulation respectively.

The progressive increase in the desflurane concentration decreased the amplitude of all spinal SSEP(Table 1). The percentage changes by 9 and 12 % desflurane to the 6 % of the spinal SSEPs are showed in Fig 2 and 3. By statistical analysis, the reduction reached a level of significant at 12 % (p=0.03, 0.02 and 0.04 in sciatic, PT, and spinal cord elicited spinal SSEPs). Comparing the effects on different spinal SSEPs, during the increased concentration administration of 9 to 6%, there is no significant difference in the degree of reduction (Fig 2). However, in 12 to 6 %, more significant profound depression of amplitude was found in PT and spinal cord elicited SSEPs (Fig 3).

Although there was an increase in latency associated the increase of the desflurane concentration, the results were not statistically significant.
Discussion

The results obtained in the present study revealed that even the success rate and amplitude of the spinal SSEP elicited by direct stimulation on the major peripheral nerve is better than those by indirect peripheral nerve or direct spinal cord stimulation during the administration of desflurane. However, the significant depression effect, expressed by the reduction of amplitude and elongation of the latency, occurred dependently to the concentration of desflurane in these three models of spinal SSEP. Desflurane, as a derivative of isoflurane, potentially, could depress the evoked potential like isoflurane and other halogenated anesthetic agents. Because of the clinical popularity is expected to be increasing\(^7\), therefore the effects on the variable intraoperative evoked potentials become important. Many articles have examined the effect of desflurane on MEP (motor evoked potential) and SSEP systemically\(^2,4,14,19\). In MEP, Haghighi and co-workers’s documented that at 5.7% desflurane, abolishment of the potential occurred in a significant rate with significant amplitude reduction.

Furthermore, in 11.4%, none of the animal had a measurable response. In the investigation of SSEP, they showed that in both cortical and spinal SSEP elicited by indirect stimulation of posterior tibial nerve were also suppressed in a dose-dependent manner. The cortical SSEP lost completely in 35% of all examined animals at 5.7% and all (100%) at 11.4% desflurane respectively; and spinal SSEP was more resistant as none (0%) and 11.1% of arts lost the response at 5.7 and 11.4% respectively.

Moreover, the significant reduction in the magnitude of amplitude during the increasing concentrations of desflurane occurred in very light concentration as 1.4% for cortical SSEP and 5.7% for spinal SSEP\(^23\). These findings are compatible with those obtained in this present study.

The amplitude of cortical SSEP was very low and requires an extremely high-fidelity amplifier and a computer system, and always needs a number of averaging to eliminate
noise and reach a definite potential. Furthermore, the cortical SSEP was very liable to be affected by anesthesia and physiologic factors\textsuperscript{4}. Moreover, when interpreting the data of response to stimulation of the lower limbs, the peaks all less pronounced than the response to stimulation of the upper limbs\textsuperscript{16,17}. Spinal SSEP, first applied to human subjective by Magladery et al in 1957, is a solution to these problems. Although no major complications has been reported, this technique was criticized to be too invasive. Therefore, the experimental investigation and the clinical experience of the spinal SSEP are less well-established than cortical SSEP. However, the issue of the spinal SSEP would become more important due to increasing popularity of the spinal SSEP monitoring over cortical SSEP. Because of the two reasons; 1. the increasing incidence of intraoperative neuromonitoring of the lower extremities because of the increasing risk brought by the more invasive surgical procedure in the lumbar spine or the hip girdle which warrant spinal SSEP in successful monitoring. 2. there was few studies was addressed the effects of anesthesia on the different spinal SSEP elicited by the different stimulation level of peripheral nerve and spinal cord. desflurane, whose cerebral washin and washout rate is more rapid than other inhalational anesthetics\textsuperscript{23}. In addition to the clinical advantage of rapid induction and recovery\textsuperscript{20}, it may also be an appropriate drug for investigating the effects of different concentrations of anesthetics on different models of evoked potentials.

The degree of reduction in amplitude in response to increased concentration of Desflurane, demonstrated here by the different stimulating models of spinal SSEP. The results showed that the spinal SSEP elicited by direct sciatic nerve stimulation is significant stable than spinal cord or indirect peripheral nerve stimulation. The finding was evidenced by the lower percentage of reduction in amplitude and the rate of abolishment of potential. The finding make it most practical to use direct stimulation on major peripheral nerve in spinal SSEP recording in proceeding the intraoperative
neuromonitoring on lumbar spinal segment or sciatic nerve. The reduction of amplitude in the posterior tibial or spinal cord stimulation from 12% Desflurane to that of 6% Desflurane was approximate to 50% in average. On theoretical grounds, the correct interpretation of amplitude reduction from actual neural damage than the change effected by anesthetics is impossible by the basis of potential change simply. In practice, reversal of the concentration and close following up of the potential can tell the difference. However, in addition to the waste of the time during surgery, this may cause unnecessary burden to the surgeons and monitor team, and may also loss the chance in prevention irreversible damage. Accordingly, if the lower extremity is to be recorded as a continuous monitoring, the standard stimulation should be on the major sciatic nerve in a more direct technique like subcutaneous needle stimulation.

Although the precise site at which the SSEPs are suppressed by desflurane is unknown, like those of the other halogenated anesthetic agents, the synaptic transmission has been regarded as the primary site of anesthesia\textsuperscript{14,20}. However, it was suggested that desflurane acts on a somewhat different locus in the central nervous system as compared to isoflurane in the investigation of CMAP (compound muscle action potential). In this study, the major, initial spike in the conductive SCEP we used was transfer through the dorsolateral column\textsuperscript{7,8}; and the synaptically induced depolization of neuron in the spinal cord was responsible for the segmental SCEP and SSEP\textsuperscript{9}. Based on the finding that both conductive and segmental SCEP of different origin, were all suppressed by the increased desflurane, as consequence, the suppressive effect may not arise on synaptic transmission only.

In this study, mean arterial pressure decreased when des was administrated in higher concentration. But, the other parameters of the physiologic factors, as heart rate, pH, O2 saturation remains normal. These results are consistent with many reports by other investigators\textsuperscript{3,6,15}. Regarding the important conclusion by Milde and Milde that
desflurane-induced hypotension decreased the cerebral brain flow and cerebral metabolic rate, however the perfusion to brain was adequate to maintain cerebral metabolic rate by their extensive study dog; des seems to be useful as a technique for producing controlled hypotension\textsuperscript{15}. Although Haghighi et al presumed hypotension is one of the factors in the CMAP amplitude reduction and latent prolongation induced by increased desflurane\textsuperscript{2}. In this study of des-induced depression of SSEP, we did not favored this possibility because of (1) the correlation of the suppression of mean arterial pressure and the SSEP is deficient, (2) the degree of blood pressure fall was not below 40 mm Hg, a criteria will suppress the SSEP demonstrated by Branson et al\textsuperscript{10}. 

References


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Figure 1. Typical waveform change of different models of spinal SSEP show an increase in latency and decrease in amplitude to different desflurane concentration.
Figure 2. Effects of different desflurane concentration on different models of spinal SSEP amplitude. (Asterisks indicate a statistically significant difference between values for 9%/6% and 12%/6% within a group; different letters indicate a statistically significant difference between values across different models of spinal SSEP groups.)
Figure 3. Effects of different desflurane concentration on different models of spinal SSEP amplitude. (Asterisks indicate a statistically significant difference between values for 9%/6% and 12%/6% within a group; different letters indicate a statistically significant difference between values across different models of spinal SSEP groups.)
Table 1.

<table>
<thead>
<tr>
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<th>Desflurane</th>
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<tbody>
<tr>
<td></td>
<td>6%</td>
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<tr>
<td><strong>Systolic P</strong></td>
<td>112.0±9.6</td>
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<tr>
<td><strong>Diastolic P</strong></td>
<td>93.6±21.6</td>
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<tr>
<td><strong>MAP</strong></td>
<td>104.1±20.1</td>
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<tr>
<td><strong>HR</strong></td>
<td>224.9±35.1</td>
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<tr>
<td><strong>pH</strong></td>
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<tr>
<td><strong>PaO₂</strong></td>
<td>41.03±7.20</td>
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<tr>
<td><strong>PaCO₂</strong></td>
<td>303.2±62.4</td>
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</tbody>
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Table 1. Hemodynamic responses to different desflurane concentration.

MAP = mean arterial pressure; HR = heart rate
<table>
<thead>
<tr>
<th>Desflurane</th>
<th>6%</th>
<th>9%</th>
<th>12%</th>
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<tbody>
<tr>
<td>PT-SSEP</td>
<td>55.2 ± 32.5</td>
<td>48.9 ± 32.2</td>
<td>35.5 ± 40.3</td>
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<tr>
<td>Sciatic-SSEP</td>
<td>166.9 ± 62.3</td>
<td>149.7 ± 65.1</td>
<td>120.1 ± 79.5</td>
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<tr>
<td>Conductive-SSEP</td>
<td>166.4 ± 122.4</td>
<td>115.0 ± 100.7</td>
<td>54.2 ± 44.2</td>
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Table 2. Amplitude (mV) of different models of spinal SSEP in response to different desflurane concentration.
Table 3. Latency (ms) of different models of spinal SSEP in response to different desflurane concentration

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<th>Desflurane</th>
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<td>6%</td>
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<tr>
<td>PT-SSEP</td>
<td>3.88 ± 0.53</td>
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<tr>
<td>Sciatic-SSEP</td>
<td>1.51 ± 0.17</td>
</tr>
<tr>
<td>Conductive-SSEP</td>
<td>1.60 ± 0.36</td>
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