

Original articles

Evaluation of the applicability of sevoflurane during post-tetanic myogenic motor evoked potential monitoring in patients undergoing spinal surgery

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Abstract

Purpose. Recent evidence has indicated that post-tetanic motor evoked potentials (p-MEPs) can be used to improve the reliability of the monitoring of motor function during spinal surgery. However, data on p-MEP monitoring are limited to those in subjects under propofol anesthesia. The present study was conducted to assess the applicability of sevoflurane during p-MEP monitoring in patients undergoing spinal surgery.

Methods. Thirty-five patients undergoing spinal surgery under sevoflurane anesthesia were enrolled in the study and classified as being without preoperative motor deficits ($n = 25$) or with preoperative motor deficits ($n = 10$). For conventional MEP (c-MEP), transcranial train-pulse stimulation was delivered and the compound muscle action potentials were bilaterally recorded from the abductor pollicis brevis, abductor hallucis, tibialis anterior, and soleus muscles. For p-MEP, tetanic stimulation (50 Hz, 50 mA stimulus intensity) for 5 s was applied to the bilateral median and left tibial nerves 1 s prior to transcranial stimulation.

Results. The amplitudes of p-MEP were significantly higher in all muscle recording sites than those of c-MEP in patients without motor deficits, whereas these amplitudes were significantly higher in only four of the eight muscles in patients with motor deficits ($P < 0.05$). The success rates of c-MEP and p-MEP recording were 48% and 64%, respectively, in patients without motor deficits and 30% and 60%, respectively, in patients with motor deficits. There were no statistically significant differences in success rates between c-MEP and p-MEP recording.

Conclusion. Although the application of tetanic stimulation prior to transcranial stimulation did not significantly increase the success rates of MEP recording, it significantly enlarged MEP amplitude under sevoflurane anesthesia in patients without preoperative motor deficits.

Key words Motor evoked potential · Sevoflurane · Tetanic stimulation · Spinal surgery

Introduction

Intraoperative neurological monitoring with myogenic motor evoked potential (MEP) provides helpful information for assessing the corticospinal tract integrity of descending motor pathways during spinal surgery in which there is a risk of spinal cord injury [1–3]. However, clinical and experimental use of MEP monitoring during spinal surgery has shown that MEP responses are significantly suppressed by most anesthetics in a dose-dependent manner, particularly volatile anesthetics [4–11]. Therefore, intravenous anesthetics such as propofol and ketamine are preferentially used during intraoperative MEP monitoring [12,13].

Recently, we developed a new technique to improve the reliability of MEP recording, called post-tetanic MEP (p-MEP), in which the MEP amplitude, compared with that of conventional MEP (c-MEP), can be enlarged by tetanic stimulation of peripheral nerves prior to transcranial electrical stimulation [14–17]. Our previous data suggested that tetanic stimulation (50 Hz, 50 mA) of peripheral nerve with a duration of 3–5 s and a post-tetanic interval of 1–5 s could be applied for the purpose of augmenting the MEP amplitude [14]. Additionally, the results of intraoperative p-MEP monitoring under propofol anesthesia during spinal surgery revealed higher success rates of baseline MEP recording, with fewer false-negative and false-positive rates than those of c-MEP [16].

In the present study we hypothesized that the application of p-MEP could overcome the suppressive effect of sevoflurane, and therefore that MEP monitoring may be feasible even under sevoflurane anesthesia. The present study was designed to investigate whether the application of p-MEP could augment the amplitude of MEP and increase the success rate of MEP recording in patients with and without preoperative motor deficits under sevoflurane anesthesia.

Patients, materials, and methods

After we had gained institutional approval for the study at Nara Medical University, Nara, Japan, written informed consent was obtained from each patient. From September 2007 to July 2008, a total of 35 American Society of Anesthesiologists physical status I or II patients undergoing elective spinal surgery were enrolled in the study. There were 21 males (60%) and 14 females (40%). Age (mean \pm SD) was 62 ± 16 years, with a range between 9 and 83 years. Diseases in these patients included cervical spinal stenosis ($n = 10$), cervical spinal tumor ($n = 1$), lumbar spinal stenosis ($n = 17$), lumbar spinal tumor ($n = 4$), and others ($n = 3$). Patients with documented seizure history, implanted atrial and/or ventricular pacemakers, cochlear implants, spinal cord stimulators, and/or pumps were precluded from participation. All patients had one or more neurological symptoms, such as back pain, intermittent claudication, or sensory and motor deficits caused by spinal cord injury. Each patient's preoperative motor state was evaluated according to a manual muscle test (MMT) performed by orthopedists. The patients were divided into two groups based on the MMT score; a normal group (MMT score of 5) and a motor-deficit group (MMT score of 2 to 4). There were no patients with an MMT score of 0 or 1.

Anesthesia was standardized in all patients. No premedication was given before anesthesia. After preoxygenation, anesthesia was induced with continuous intravenous infusion of remifentanyl ($0.2 \mu\text{g}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$) and propofol ($1\text{--}1.5 \text{mg}\cdot\text{kg}^{-1}$). The trachea was intubated after succinylcholine ($1.5 \text{mg}\cdot\text{kg}^{-1}$) was administered. Muscle relaxants were not used after intubation. Anesthesia was maintained with sevoflurane and remifentanyl ($0.2 \mu\text{g}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$). Sevoflurane was maintained at an end-tidal concentration of 1.3% by using a Nihon Kohden respiratory gas monitor (BSS-9800; Nihon Kohden, Tokyo, Japan). After intubation, semiclosed circuit mechanical ventilation was adjusted to maintain

end-tidal carbon dioxide tension between 35 and 40 mmHg, using tidal volume set at $8\text{--}12 \text{ml}\cdot\text{kg}^{-1}$ and a rate of $8\text{--}12 \text{breaths}\cdot\text{min}^{-1}$. The patient's rectal temperature was maintained between 35.5 and 37.0°C with warming blankets. Patients were monitored with electrocardiogram, finger pulse oximeter probe, automatic blood pressure cuff, and bispectral index values (BSS-9800; Nihon Kohden). Mean arterial pressure was maintained between 70 and 100 mmHg throughout the operation.

Technique for c-MEP and p-MEP recording

c-MEP

For recording c-MEP, transcranial electrical stimulation was generated with a multiple stimulator (D-185; Digitimer, Welwyn Garden City, UK). A train-of-five square-wave pulses was delivered at an interstimulus interval of 2 ms (500 Hz). The stimulating electrodes consisted of a pair of 14.5-mm silver-plated disk electrodes at C3 (cathode) and C4 (anode) (motor cortex areas in the International 10–20 system) affixed with conductive paste. The stimulus intensity of transcranial stimulation was determined at the beginning of MEP recording and was set just supramaximal to each stimulus (approximately 500 V; Fig. 1). The compound muscle action potentials were bilaterally recorded from the skin over the abductor pollicis brevis (APB), abductor hallucis (AH), tibialis anterior (TA), and soleus (S) muscles. A ground electrode was placed on the left or right arm proximal to the elbow. An intraoperative MEP measurement system (Neuropack MEB-2208; Nihon Koden) was used for MEP monitoring.

p-MEP

Tetanic stimulation (50 Hz, 50 mA stimulus intensity) with a duration of 5 s was applied to the bilateral median nerves at the wrist and left tibial nerves at the ankles 1 s prior to transcranial electric stimulation. Transcranial electrical stimulation was automatically triggered

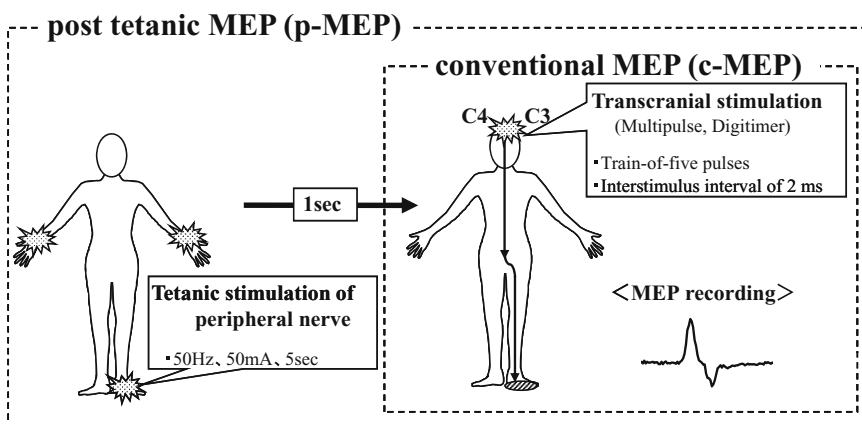


Fig. 1. Technique to record post-tetanic motor evoked potential (*p-MEP*) and conventional MEP (*c-MEP*). For *c-MEP* recording, transcranial stimulation was performed by train-of-five pulses with an interstimulus interval of 2 ms to C3 and C4 (international 10–20 system) and the compound muscle action potentials were recorded. For *p-MEP* recording, tetanic stimulation of the left tibial nerve with a duration of 5 s and a stimulus intensity of 50 mA at 50 Hz was performed prior to transcranial stimulation with a posttetanic interval of 1 s

after the application of tetanic stimulation. Transcranial electrical stimulation was performed in the same manner as that described for c-MEP recording (Fig. 1). The compound muscle action potentials were recorded from the same muscles as those used for c-MEP recording.

Study protocol

Both c-MEP and p-MEP were recorded during the surgical procedure, once a steady anesthetic state was established. First, c-MEP and then p-MEP were recorded as the baseline approximately 45 min after intubation. Peak-to-peak amplitude was determined from the average of two individual responses. In our preliminary study, we had determined that an interval of 2 min after p-MEP recording did not affect subsequent MEP responses, so that the interval after p-MEP recording was set at more than 2 min to avoid an interaction. When the MEP amplitude was more than 30 mcV, MEP recording was defined as successful. The criteria for significant change were defined as a persistent amplitude decrease to less than 30 mcV or a value of more than 75% of the baseline.

Statistical analysis

Comparisons of amplitudes between c-MEP and p-MEP at each recording site were performed using Wilcoxon's signed rank test. Success rates of baseline c-MEP and p-MEP recording were compared using the χ^2 test. *P* values of less than 0.05 were considered significant.

Results

Skin burns at stimulation sites, cardiac arrhythmias, intraoperative or postoperative seizures or epilepsy episodes related to repetitive peripheral and transcranial electrical stimulation were not observed in any patient. Bispectral index values for all patients were stable, at a range of 40–60, throughout the operation.

Of the 35 patients, 25 had no preoperative motor deficit, whereas 10 patients had a preoperative motor deficit. Comparisons of baseline amplitudes between c-MEP and p-MEP are shown in Figs. 2 and 3. In the patients without preoperative motor deficits, the amplitudes of p-MEP from all muscle recording sites were significantly higher than those of c-MEP. In contrast, in patients with preoperative motor deficits, the amplitudes of p-MEP from the right APB, bilateral AH, and right TA muscles, but not the other four muscles, were significantly higher than those of c-MEP.

The success rates of MEP recording from all muscles are shown in Table 1. In the 25 patients without a preoperative motor deficit, baseline c-MEP and p-MEP responses from all muscle recording sites were recorded in 48% and 64%, respectively. In the 10 patients with preoperative motor deficits, baseline c-MEP and p-MEP responses from all muscle recording sites were recorded in 30% and 60%, respectively. The patients without reliable p-MEP responses also had no reliable c-MEP responses. The success rates of p-MEP in patients with and without preoperative motor deficits were higher than those of c-MEP, but there were no significant differences in success rates between c-MEP

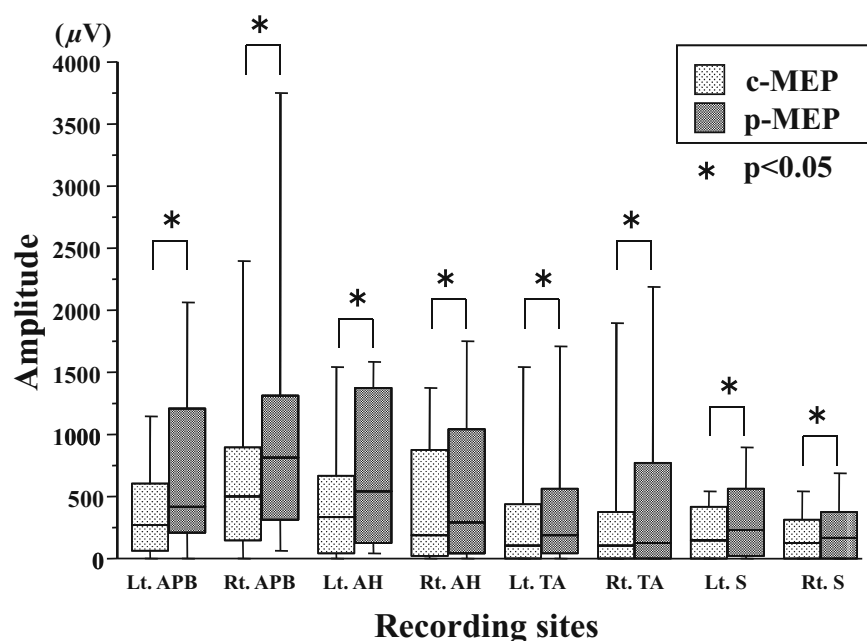


Fig. 2. Comparisons of amplitudes of c-MEP and p-MEP from the bilateral abductor pollicis brevis (APB), abductor hallucis (AH), tibialis anterior (TA), and soleus (S) muscles in patients without preoperative motor deficits. The amplitudes of p-MEP from all muscle recording sites were significantly higher than those of c-MEP. *Lt*, Left; *Rt*, right. **P* < 0.05 (c-MEP vs p-MEP)

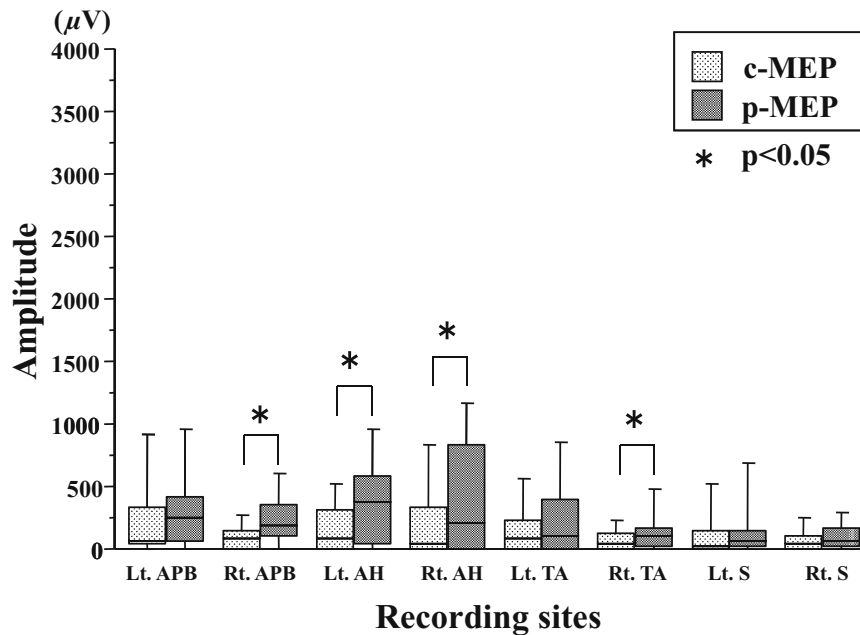


Fig. 3. Comparisons of amplitudes of c-MEP and p-MEP from the bilateral abductor pollicis brevis (APB), abductor hallucis (AH), tibialis anterior (TA), and soleus (S) muscles in patients with preoperative motor deficits. The amplitudes of p-MEP from the right (Rt) APB, bilateral AH, and right TA muscles, but not the other four muscles, were significantly higher than those of c-MEP. * $P < 0.05$ (c-MEP vs p-MEP)

Table 1. Success rates of motor evoked potential (MEP) recording from all muscles in patients without and with motor deficits

	Without motor deficits ($n = 25$)		With motor deficits ($n = 10$)	
	c-MEP	p-MEP	c-MEP	p-MEP
Lt. APB	80% (20/25)	88% (22/25)	80% (8/10)	80% (8/10)
Rt. APB	80% (20/25)	92% (23/25)	70% (7/10)	80% (8/10)
Lt. AH	88% (22/25)	92% (23/25)	50% (5/10)	80% (8/10)
Rt. AH	76% (19/25)	80% (20/25)	50% (5/10)	60% (6/10)
Lt. TA	64% (16/25)	76% (19/25)	60% (6/10)	70% (7/10)
Rt. TA	68% (17/25)	72% (18/25)	50% (5/10)	70% (7/10)
Lt. S	64% (16/25)	76% (19/25)	40% (4/10)	70% (7/10)
Rt. S	64% (16/25)	72% (18/25)	60% (6/10)	70% (7/10)
All muscles	48% (12/25)	64% (16/25)	30% (3/10)	60% (6/10)

For c-MEP and p-MEP recording, the compound muscle action potentials were recorded from the bilateral abductor pollicis brevis (APB), abductor hallucis (AH), tibialis anterior (TA), and soleus (S) muscles in patients without and with preoperative motor deficits. When the MEP amplitude was less than 30 mcV, the MEP response was defined as “no response”. The success rate for “all muscles” indicates the percentage of patients with MEP responses from all muscle recording sites

and p-MEP. No patients had significant intraoperative changes in MEP responses and no new postoperative neurological deficits were observed in any patients.

Discussion

The results in the present study show that the application of p-MEP augmented the amplitudes of MEP from all muscle recording sites in patients without preoperative motor deficits, whereas p-MEP augmentation was observed in four of eight muscle recording sites in

patients with preoperative motor deficits. The application of p-MEP increased the success rates from 48% to 64% in patients without preoperative motor deficits and from 30% to 60% in patients with preoperative motor deficits, compared with c-MEP, under sevoflurane and remifentanyl anesthesia without neuromuscular blockade during spinal surgery.

Tetanic stimulation of peripheral nerves has been widely used as a method to potentiate muscle response during neuromuscular blockade [18,19]. During the administration of a nondepolarizing neuromuscular blocking agent, tetanic nerve stimulation at 50–100 Hz

is followed by a post-tetanic increase in twitch tension (i.e., post-tetanic fasciculation of transmission). The post-tetanic count after tetanic stimulation at 50 Hz for 5 s has therefore become an accepted technique to quantify the degree of intense neuromuscular block under the condition in which responses to single-twitch stimulation are no longer obtained [20–22]. Kakimoto et al. [14] hypothesized that the application of tetanic stimulation to peripheral nerves prior to transcranial stimulation might augment the amplitudes of MEPs from the muscles that were innervated by the nerve subjected to the tetanic stimulation. These authors [14] found that the application of tetanic stimulation to peripheral nerves at a stimulus intensity of 25–50 mA with a duration of 3–5 s and a post-tetanic interval of 1–5 s significantly augmented the amplitudes of MEPs in patients under propofol/fentanyl anesthesia with partial neuromuscular blockade during spinal surgery.

Subsequent studies from our laboratory have indicated that the application of tetanic stimulation to a peripheral nerve at one site could also augment the amplitudes of MEPs from muscles that were not innervated by the nerve subjected to the tetanic stimulation, in patients without preoperative motor deficits under propofol/fentanyl anesthesia with partial neuromuscular blockade during spinal surgery [15]. This finding and the data from previous studies suggested that, as mechanisms of the MEP augmentation produced by tetanic stimulation of peripheral nerves, corticomotoneuronal excitability at the level of brain and spinal cord might be also involved [23–26]. In the present study, tetanic stimulation was applied to the bilateral median nerves at the wrist and the left tibial nerve at the ankle at the same time. Theoretically, it would be better to apply tetanic stimulation to the bilateral upper and lower limbs to obtain the maximal augmentation of MEPs. However, the machine we used can deliver stimulation to only three sites at the same time. Although this stimulus setup may not be optimal, based on our clinical experience, MEP amplitudes from the muscles in the bilateral upper and lower limbs could be augmented, at least in patients under propofol-based anesthesia.

The use of sevoflurane as an anesthetic during MEP monitoring has been precluded because it has more suppressive effects on MEPs compared with those of intravenous anesthetics such as propofol and ketamine, although the data on the effects of sevoflurane on MEPs are limited. Kawaguchi et al. [6] reported the effects of sevoflurane on MEPs elicited by single and paired transcranial electrical stimulation during spinal surgery. During the administration of 0.5 and 0.75 minimum alveolar concentration (MAC) sevoflurane, MEPs induced by single pulse stimulation could be recorded in only 22% and 0% of patients, respectively.

Although the application of paired pulses for stimulation significantly increased MEP amplitudes compared with those achieved by single pulse stimulation, the success rates of MEP recording were still low even after the application of paired pulses (56% and 11% during 0.5 and 0.75 MAC sevoflurane, respectively), suggesting that paired stimuli were not sufficient to overcome the depressive effects of sevoflurane at clinically used concentrations.

Recently, Reinacher et al. [27] investigated the effects of different stimulation patterns and end-tidal concentrations of sevoflurane on intraoperative transcranial electrical MEPs; they demonstrated that, although sevoflurane modified MEP amplitudes in a dose-dependent manner, a train of four to five pulses at 1000 Hz allowed intraoperative MEP recording during up to 1 MAC sevoflurane in patients undergoing supratentorial craniotomy. The success rates of MEPs from the thenar muscles were 100% and 92% under 0.75 MAC and 1 MAC, respectively, in patients with intact motor tracts. These findings suggested that MEP monitoring may be feasible under sevoflurane anesthesia, if stimulation patterns were modified. In the present study, the success rates of c-MEP and p-MEP recordings were 48% and 64%, respectively, in patients without preoperative motor deficits, and 30% and 60%, respectively, in patients with preoperative motor deficits. The success rates of c-MEPs and p-MEPs obtained in the present study seem to be lower than those reported by Reinacher et al. [27]. The reasons for these differing results are unknown. However, some possible explanations are as follows. First, the subjects differed between the studies. Reinacher et al. [27] evaluated patients undergoing supratentorial craniotomy who had no preoperative motor deficits, whereas in the present study, patients with one or more clinical symptoms such as back pain, intermittent claudication, and motor deficits caused by spinal injury were included. Second, Reinacher et al. [27] recorded the MEPs only from the upper limbs, whereas MEPs from both the upper and lower limbs were recorded in the present study. Third, the stimulus frequency differed between the studies. Reinacher et al. [27] reported that maximal MEP success rates were achieved at a stimulus frequency of 1000 Hz, whereas these rates were achieved at a stimulus frequency of 500 Hz in the present study.

In our previous study, we compared the success rates of c-MEP and p-MEP recording under propofol anesthesia in 80 patients undergoing spinal surgery [16]. The results indicated that the success rates of c-MEP and p-MEP recording were 74.5% and 96.1%, respectively, in patients without preoperative motor deficits, whereas the success rates of c-MEP and p-MEP recording were 51.7% and 86.2%, respectively, in patients with preop-

erative motor deficits. Considering the results obtained under propofol anesthesia in that previous study, the success rates of c-MEP and p-MEP recording under sevoflurane anesthesia, obtained in the present study, are lower than those obtained under propofol anesthesia in patients without and with preoperative motor deficits. These findings suggest that sevoflurane anesthesia seems likely to have no additional benefits beyond propofol anesthesia in terms of monitoring c-MEPs and p-MEPs during spinal surgery.

There are several limitations of the present study that merit comment. First, in this study we used an end-tidal sevoflurane concentration of 1.3%. Although we selected this concentration in order to avoid intraoperative awareness, the success rates of p-MEP recording may have been higher if a lower concentration of sevoflurane had been used. Second, in the present study, transcranial stimulation was performed using a train of five pulses at a stimulus frequency of 500 Hz and a stimulus intensity of approximately 500 V, based on the data from our previous study carried out in patients under propofol anesthesia. However, different stimulus patterns may be optimal to achieve maximal MEP amplitudes and success rates under sevoflurane anesthesia. Finally, the number of patients enrolled in the present study was relatively small. Although the accrual of more patients would be required to reach conclusions on the applicability of sevoflurane during p-MEP monitoring, we terminated the study because we considered that sevoflurane had no additional benefits beyond propofol during spinal surgery, especially in patients with preoperative motor deficits.

In summary, we investigated whether the application of p-MEP could overcome the suppressive effect of sevoflurane and therefore whether MEP monitoring may be feasible even under sevoflurane anesthesia during spinal surgery. The results of this study showed that p-MEP can be effectively used as a method to augment the amplitudes of MEP in patients under sevoflurane anesthesia, especially in those patients without preoperative motor deficits. Although the application of p-MEP increased the success rates of MEP recording compared with those of c-MEP, the increase was not statistically significant and the success rates of p-MEP recording under sevoflurane anesthesia did not seem to reach an adequate level for clinical use. Considering the results in the present and previous studies, it is suggested that propofol may be a better choice than sevoflurane anesthesia for anesthetic management during c-MEP and p-MEP monitoring in patients undergoing spinal surgery. However, the present study was not designed to compare MEP results between propofol and sevoflurane. To reach conclusions on the applicability of sevoflurane during MEP monitoring, further study would be required.

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