Does Somatosensory-Evoked Potential Simultaneously Decrease with Transcranial Motor-Evoked Potential Alarm? A Multicenter Study by the Monitoring Committee of the Japanese Society for Spine Surgery and Related Research

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Abstract:

Introduction: Multimodal intraoperative neurophysiological monitoring (IONM)―such as monitoring muscle-evoked potentials after transcranial electrical stimulation (Tc-MEP) with somatosensory-evoked potential (SEP) after electrical stimulation of the peripheral nerve―is recommended in spine surgeries to prevent iatrogenic neurological complications. However, the effect of using Tc-MEP with SEP to protect against neurological complications, particularly motor function, remains unknown. In clinical settings, changes due to Tc-MEP meeting the alarm points must be a potential neurological injury. This retrospective study, focusing on true-positive (TP) cases, aimed to clarify the change in the SEP waveform simultaneously with the Tc-MEP alarm.

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Methods: We included 68 patients with TP who had Tc-MEP changes and new postoperative motor weakness at more than one level of the manual muscle test after surgery. We compared the cases based on the category of spine surgery and paralysis type. We evaluated sex, age at spine surgery (high- or non high-risk), and paralysis type (segmental, long tract, or both). We defined the alarm points as follows: >70% decrease in Tc-MEP wave amplitudes, >50% decrease in wave amplitudes, or 10% extension of SEP latency. Next, we evaluated the SEP wave changes with a Tc-MEP alarm.

Results: All patients showed progressive motor weakness after surgery, and 21 patients (31%) showed SEP changes at the same time as the Tc-MEP alarm. There were no statistically significant differences in the ratio of SEP change between the two groups according to the spine surgery category or among the three groups according to the paralysis type.

Conclusions: Multimodal IONM is an important tool. However, the SEP changes do not necessarily appear immediately after the Tc-MEP alarm. Spine surgeons should appropriately treat Tc-MEP alarms to preserve motor function, regardless of SEP changes.

Keywords:

Tc-MEP, SEP, alarm point, wave amplitude, latency, high-risk spine surgery

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Introduction

Spinal surgery carries a risk of injury to critical neural structures. The rate of surgery-related neurological deterioration ranges from 1.4% among surgeries for all spinal disorders[1] to 32.0% among surgeries for thoracic ossification of the posterior longitudinal ligament (OPLL)[2]. Neurological complications may occur because of direct mechanical force applied to the spinal cord during intervention or indirect ischemic changes such as cord distraction/compression during corrective maneuvers[3]. Intraoperative neurophysiological monitoring (IONM) is crucial for preventing spinal cord or nerve root injuries during spinal surgery.

IONM can be performed using several modalities, such as muscle-evoked potential after transcranial electrical stimulation of the brain (Tc-MEP), somatosensory-evoked potential (SEP) after electrical stimulation of the peripheral nerve, spinal cord-evoked potential after transcranial electrical stimulation of the brain (D-wave), spinal cord-evoked potential after stimulation of the spinal cord, spontaneous electromyography (EMG; free-run EMG), triggered EMG, and muscle-evoked potential after electrical stimulation of the spinal cord. Tc-MEP is the most frequently used technique to assess motor pathway damage in Japan[4], and SEP is used to assess sensory pathway damage. Tc-MEP and SEP complement each other in interpreting monitoring to protect neurologic structures. Although SEP primarily monitors the sensory pathway, it is sometimes used as a motor pathway monitoring tool[5]. We recommend using multimodal IONM to prevent intraoperative neurological complications, such as Tc-MEP with SEP[6].

However, the use of Tc-MEP with SEP to protect against neurological complications, particularly motor function, remains unknown. Considering the risk of neurological complications, we categorized neurological complications as non high-risk spine surgery cases and spinal deformity, cervical ossification posterior longitudinal ligament (OPLL), thoracic OPLL, intradural extramedullary spinal cord tumor, and intradural intramedullary spinal cord tumor cases as high-risk spine surgery cases.

The efficacy of Tc-MEP with D-waves has been confirmed, and this multimodal combination reduces the false-positive case rate and increases IONM sensitivity and specificity[7]. When focusing on Tc-MEP alarm timing, spinal surgeons must determine how to treat such situations as early as possible. Considering the utility of Tc-MEP with SEP for motor function, we determined whether SEP monitoring could detect abnormalities immediately after the Tc-MEP alarm, such as by a decreased wave amplitude and/or prolonged latency. Thus, we aimed to clarify SEP wave changes during the Tc-MEP alarm to determine the differences in SEP wave changes among spine disorders and clarify the differences in SEP wave changes among paralysis types. We hypothesized that SEP wave changes occur at the alarm point for Tc-MEP, particularly in high-risk spine surgeries, and speculated that spinal cord damage tends to occur cross-sectionally, particularly during high-risk spinal surgery. For further understanding, we performed a subgroup analysis to clarify the changes in SEPs based on the type of postoperative motor paralysis, including segmental, long tract, and both.

Materials and Methods

This study was approved by the ethics committee of our institution (approval code: 3626). Patients and their parents provided informed consent.

Patients

The Spinal Cord Monitoring Working Group of the Japanese Society for Spine Surgery and Related Research conducted this retrospective, multicenter cohort study, including 7,299 patients who underwent Tc-MEP monitoring during spinal surgery at 14 spinal centers between April 2017 and March 2021. However, patients with a history of epilepsy were excluded. The database excluded any information on sensory disturbances from the pre- to post-operative periods.

To test our hypothesis, we focused on TP cases, defined as a Tc-MEP alarm with a persistent decrease in the number of potentials at the end of the operation, followed by the observation of a new neurological motor deficit after the operation (manual muscle test of more than one grade). Based on a previous study, we defined high-risk surgeries as spinal deformities, cervical OPLL, thoracic OPLL, extramedullary spinal cord tumors, and intramedullary spinal cord tumors[8]. In addition, we categorized cervical spondylotic mylopathy, lumbar spinal canal stenosis, cauda equina tumor, and trauma cases as non high-risk surgeries in this study.

We defined segmental paralysis as motor paralysis limited to a surgical site, such as C5 nerve palsy after cervical laminoplasty and defined long tract paralysis as broad motor paralysis extending from the surgical site.

Anesthesia

All procedures were performed under total intravenous anesthesia with propofol (3-4 mg/mL) and fentanyl (2 mg/kg) administration. Propofol (100-150 mg/kg/min) and remifentanil (1 mg/kg/h) were used to maintain anesthesia with a bispectral index of 40-60. Vecuronium (0.12-0.16 mg/kg) was used as a muscle relaxant during intubation, and the antagonist was used when the train-of-four ratio was <0.6. Systolic blood pressure and body temperature were >90 mmHg and >35°C, respectively.

Tc-MEP monitoring

Corkscrew-type stimulating or silver-silver chloride electrodes were placed bilaterally and symmetrically 5 cm lateral and 2 cm anterior to the Cz (international 10-20 electrode placement system). Constant voltage and current stimulators were used. For constant-current stimulators, the transcranial stimulus parameters were as follows: 5-10 train stimuli, a stimulus interval of 2 ms, intensity of 100-200 mA, duration of 0.5 ms, filter of 2-3 kHz, and recording time of 100-200 ms. In contrast, for constant-voltage stimulators, the transcranial stimulus parameters were as follows: 5 train stimuli, a stimulus interval of 2 ms, intensity of 300-600 V, duration of 0.05 ms, filter of 2-3 kHz, and recording time of 100-200 ms.

Muscle-evoked potentials were recorded from the deltoid, biceps, triceps, abductor pollicis brevis, quadriceps femoris, hamstring, tibialis anterior, gastrocnemius, and abductor hallucis muscle groups via needle or disc electrodes. The muscle-evoked potential the amplitudes were measured as baseline-to-first negative peak voltages, with amplitudes before the invasive procedure were regarded as baseline values. All muscle-evoked potential amplitude recordings were obtained using the IONM system (Neuromaster, Nihon Koden, Tokyo, Japan).

SEP monitoring (lower limb SEPs)

Herein, all true-positive (TP) cases with SEP were lower limb SEP. The SEP-stimulating electrodes were anchored laterally and caudally to the medial malleolus to excite the posterior tibial nerve. The SEP recording electrodes were positioned at Fz, CPz, CP1, and CP2 in accordance with the International 10-20 system of electrode placement. The recording points were CPz-Fz, CPz-A2, CP1-Fz, and CP2-Fz. The stimulus parameters had an intensity of 30-60 mA, a duration of 0.2-1.0 ms, and a frequency of 2-5 Hz. The recording parameters were a sensitivity of 10-20 μV/division, a low-cut filter of 1-30 Hz, a high-cut filter of 1.5-3 kHz, and an analyzed time of 60-100 ms. Each evoked potential was superimposed at least 200-1,000 times.

Definition of the alarm point regarding Tc-MEP and SEP

We set an acute decrement in the amplitude of the compound muscle action potential (CMAP) response of ≥70% from baseline as the alarm threshold based on a previous study[9]. Simultaneously, CMAPs decreased and we checked the SEP changes. An increase in the P37 wave latency of the lower extremity by 10% or an amplitude decrease of 50% when compared with the baseline value was considered an SEP alarm point.

Clinical assessment

We selected sex, age, surgery time, blood loss, postoperative motor paralysis type, and spinal disease category as our clinical assessment factors. We did not include any information on sensory deterioration or postoperative deficits.

Statistical analysis

Statistical Package for Social Sciences software (SPSS Inc., Armonk, NY) was used for statistical analysis. Unpaired continuous variables were compared using the Mann-Whitney U test, and categorical data were evaluated using the χ^2 test or Fisher's exact test. First, we divided all cases per the surgery type into high- or non high-risk groups. Second, we compared the data between the two groups in Analysis 1 (Fig. 1). Third, we divided all cases per the paralysis type—such as segment, long tract, and both—based on the surgical site and muscles with newly occurring postoperative weakness (Fig. 2). Fourth, we compared the data among the three groups in Analysis 2. Finally, we used variance analysis, a post hoc test to compare the three groups, and a Kruskal-Wallis test for continuous variables.

Results

Of 7,299 patients who underwent spinal surgeries with Tc-MEPs between 2017 and 2021, 155 patients showed TPs (2.1%) and 106 underwent SEP monitoring using Tc-MEPs. We excluded 38 patients with inadequate data, such as poor baseline waveform derivation on SEP during surgery or a lack of data regarding SEP monitoring immediately after the Tc-MEP alarm points. Finally, we analyzed 68 patients (Fig. 1) and found that 21 patients (31%) showed SEP wave changes immediately after the Tc-MEP alarm.

Analysis 1 (category of surgery)

We recorded data from 47 high-risk and 21 non high-risk patients (Fig. 2). There were 11 surgeries for high-risk patients to rectify spinal deformities (adults and pediatric), 4 cervical OPLL, 6 thoracic OPLL, 14 extramedullary spinal cord tumor, and 12 intramedullary spinal cord tumor surgeries. There were no statistically significant differences in demographic data between the two groups, except for sex and surgical time (Table 1). Regarding the change in the ratio of SEP monitoring changes immediately after the Tc-MEP alarm, no statistically significant differences were found between the two groups. Furthermore, regarding SEP changes, we found no statistically significant differences between the two groups.

Analysis 2 (paralysis types)

We recorded three groups based on the paralysis types: segment (n=26), long tract (n=39), and both paralysis types (n=3; Fig. 3). There were no statistically significant differences in the demographic data or the ratio of SEP monitoring changes immediately after the Tc-MEP alarm (Table 2).

Discussion

Herein, 21 cases (31%) showed apparent alarm for SEP simultaneously as Tc-MEPs. Although the apparent change in SEP monitoring was initially expected to occur simultaneously with the Tc-MEP alarm, particularly in high-risk spine surgery, there were no statistically significant differences in the ratio of SEP monitoring changes between high-risk and non high-risk spine surgery. Furthermore, no statistically significant differences were found in the SEP wave changes among the types of postoperative paralysis.

The primary goal of IONM is to identify patients with impending neurological damage early during surgery and manage it at the earliest using multidisciplinary approaches. Tc-MEPs are the gold standard because of their high sensitivity to motor function[10,11]. However, the false-positive rate for this modality remains relatively high[12], implying that false-positive alarms may interfere with surgery progress.

SEP, recorded from the cerebral sensory area by stimulating the peripheral nerve or skin, has been used in Europe and North America since the early 1970s[13,14]. SEP reflects dorsal column function but is relatively poor at predicting focal injury to spinal cord motor pathways[15], the most important of which is the lateral corticospinal tract. Hence, SEP carries the risk of false-negative results from the postoperative deterioration viewpoint of motor function. Conversely, SEP has shown high potential in predicting the occurrence of neurological deficits, including new motor, sensory, bowel, and bladder deficits[5]. Moreover, the overall false-negative results seemed low (0.127%) according to a survey of American surgeons[16]. Therefore, we expected a SEP change at the same time as the alarm point of the Tc-MEP in this study. However, our results did not support our hypothesis.

According to the tract within the spinal cord, SEP covers the dorsal column function, and Tc-MEPs cover the spinal

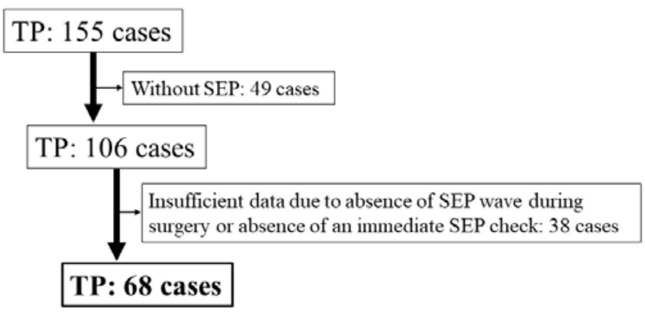

Figure 1. Patient enrollment and inclusion; TP, true positive; SEP, somatosensory-evoked potential.

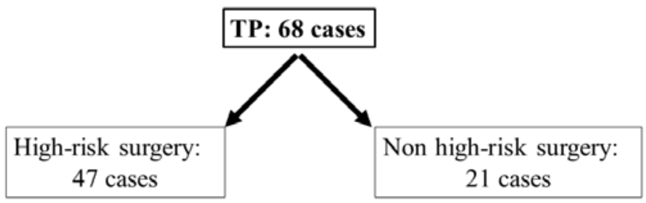

Figure 2. Case classification based on the spine surgery type; TP, true positive.

Table 1. Demographic Data Based on Surgery Category.

		High-risk (n=47)		Non high-risk (n=21)		
		Median	IQR	Median	IQR	p-value
Age (years)		64.0	52.0–73.0	70.0	53.5–75.5	0.227
Sex (n)	Male	13		12		0.029
	Female	34		9		
Surgery	Time (min)	337	260–420	269	201.5–385.5	0.026
	Bleeding (mL)	253	160–627	400	142.5–587.5	0.884
SEP change (n)		16		5		0.571
Details (n)	Latency extension	6		1		0.455
	Wave amplitude decrease	8		4		
	Both	2		0		

IQR, interquartile range; SEP, somatosensory-evoked potentials after electrical stimulation of the peripheral nerve cord motor pathways and lateral corticospinal tracts. If iatrogenic spinal cord damage occurred cross-sectionally in our TP cases, we could find SEP changes at the same time as the Tc-MEP alarm point. However, our results do not support this hypothesis. Regardless of high- or non high-risk spine surgery, some patients with TP potentially had spinal cord damage only in the lateral corticospinal tract and/or anterior horn cells, without dorsal column damage. In fact, several instances have been reported in which postoperative neurological deficits were found despite normal intraoperative SEP[16]. SEPs alone may be ineffective in detecting a motor tract deficit[9,10]. Mechanical injury, vascular supply, or hypotensive anesthesia can cause motor deficits without concomitant sensory changes during neuromonitoring. For spinal cord ischemia, Dong et al.[17] reported delayed SEP wave alterations after significant changes in the Tc-MEP during aortic aneurysm surgery. Furthermore, Hilibrand et al.[18] reported a temporal relationship between the Tc-MEP and SEP amplitude changes during cervical spine surgery. SEP signal alterations lagged behind those of Tc-MEP by an average of 16 min. Although there is no explanation for this phenomenon, these findings may explain our results.

In this study, SEP wave changes did not always occur immediately after the Tc-MEP alarm point, particularly in TP cases. However, we could not conclude whether Tc-MEP combined with SEP helped prevent new neurological deficits because we lacked information on sensory deterioration. We may need to consider that Tc-MEP with SEP is the multimodal IONM that combines with a single modality; one for motor and other for sensory function. Consequently, spine surgeons primarily focus on Tc-MEP alarms to prevent new neurological motor deficits following surgery. In particular, surgeons respond appropriately during the Tc-MEP alarm by raising blood pressure[18,19], checking surgical maneuvers or anesthetic agents[8].

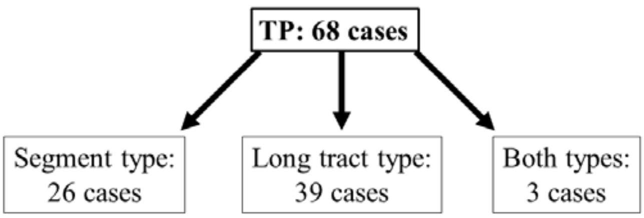

Figure 3. Case classification based on the paralysis type; TP, true positive.

Our study had some limitations. First, neurological deficits broadly include motor and sensory paralysis. Our database contained information regarding motor function pre- and post-operatively; therefore, we could not evaluate the change in sensory disturbances from pre- to post-operative. Although SEP was originally used to monitor sensory function, Tc-MEP changes with concomitant SEP changes potentially represent a specific finding correlating with subsequent neurological deteriorations than Tc-MEP changes alone. Although Tc-MEP changes that meet the predefined threshold for alarm must be considered a potential neurological injury and troubleshot accordingly, simultaneous SEP decrement should assure surgeon with increased confidence that the changes are potentially clinically significant. Further prospective studies, including sensory function, are required to confirm this hypothesis. Moreover, because of the retrospective study design, some patients did not have data on SEP wave amplitudes or latency immediately after the Tc-MEP alarm. Despite these limitations, we included many TP cases, substantially impacting our results.

Multimodal IONM should be indicated or recommended for all spinal surgeries despite the potential risk of damage to the neural structures. However, attention should be paid to SEP wave changes while assessing postoperative motor deficits. We focused on TP cases and evaluated SEP wave changes, which did not always occur simultaneously with the Tc-MEP alarm. Therefore, regardless of SEP wave changes, spine surgeons should treat Tc-MEP alarms accordingly to prevent postoperative motor deterioration, including a decrease in wave amplitude and extended latency.

Conflicts of Interest: The authors declare that there are no relevant conflicts of interest.

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Author Contributions: All authors contributed to the study conception and design. Material preparation and data

Table 2. Data Based on the Paralysis Type.

		Segment type (n=26)		Long tract type (n=39)		Both type (n=3)		
		Median	IQR	Median	IQR	Median	IQR	p-value
Age (years)		71.0	63.0–75.0	62.0	47.5–70.5	55.0	53.5–60.5	0.067
Sex (n)	Male	12		12		1		0.45
	Female	14		27		2		
Category (n)	High-risk	15		29		3		0.18
	Non high-risk	11		10		0		
Surgery	Time (min)	347.0	281.0–419.0	300.0	231.5–388.5	330.0	326.5–387.5	0.345
	Bleeding (mL)	447.0	155.0–796.0	224.0	165.0–442.5	330.0	245.0–340.0	0.38
SEP change positive (n)		7		13		1		0.86

IQR, Interquartile Range

collection were performed by H.S., G.Y., H.U., K.K., N.T., M.F., S.K., J.H., M.A., S.T., M.T., N.S., H.N., S.I., S.M., K.Y., T.T., T.K., Y.F., H.I., K.W., N.Y., K.K., A.Y., K.N., Y.T., Y.M., and K.T. Data analysis was performed by H.S. The first draft of the manuscript was written by H.S. All authors commented on the previous versions of the manuscript, and all authors read and approved the final manuscript.

Ethical Approval: This study was approved by the ethics committee of our institution (approval code: 3626).

Informed Consent: Patients and their parents provided informed consent.

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