
Clinical article

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Object. Although multimodal intraoperative spinal cord monitoring provides greater accuracy, transcranial electrical stimulation motor evoked potential (TcMEP) monitoring became the gold standard for intraoperative spinal cord monitoring. However, there is no definite alarm point for TcMEPs because a multicenter study is lacking. Thus, based on their experience with 48 true-positive cases (that is, a decrease in potentials followed by a new neurological motor deficit postoperatively) encountered between 2007 and 2009, the authors set a 70% decrease in amplitude as the alarm point for TcMEPs.

Methods. A total of 959 cases of spinal deformity, spinal cord tumor, and ossification of the posterior longitudinal ligament (OPLL) treated between 2010 and 2012 are included in this prospective multicenter study (18 institutions). These institutions are part of the Japanese Society for Spine Surgery and Related Research monitoring working group and the study group on spinal ligament ossification. The authors prospectively analyzed TcMEP variability and pre- and postoperative motor deficits. A 70% decrease in amplitude was designated as the alarm point.

Results. There were only 2 false-negative cases, which occurred during surgery for intramedullary spinal cord tumors. This new alarm criterion provided high sensitivity (95%) and specificity (91%) for intraoperative spinal cord monitoring and favorable accuracy, except in cases of intramedullary spinal cord tumor.

Conclusions. This study is the first prospective multicenter study to investigate the alarm point of TcMEPs. The authors recommend the designation of an alarm point of a 70% decrease in amplitude for routine spinal cord monitoring, particularly during surgery for spinal deformity, OPLL, and extramedullary spinal cord tumor.

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Key words • spinal cord monitoring • motor evoked potential • alarm point • technique

Abbreviations used in this paper: MEP = motor evoked potential; MMT = manual muscle testing; OPLL = ossification of the posterior longitudinal ligament; TcMEP = transcranial electrical stimulation MEP.

Neurological complications occur in 1.7% of spinal operations, which are among the most frequent surgical complications in Japan. In 2011, the Scoliosis Research Society Morbidity and Mortality Committee reported that the neurological complication
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The risk of neurological complications during surgery for thoracic ossification of the posterior longitudinal ligament (OPLL) is extremely high; Matsumoto et al. reported that the incidence of neurological complications was 26%. Matsuyama et al. reported a rate of 31% for neurological deterioration after surgery for intramedullary spinal cord tumors. As neurological complications represent one of the most serious complications, care needs to be taken to prevent perioperative neurological injury, particularly regarding spinal OPLL, spinal cord tumor, and scoliosis surgery.

Recent reports have shown that multimodal intraoperative spinal cord monitoring can reduce neurological deterioration and provide increased accuracy in the detection of spinal cord injury. In particular, transcranial electrical stimulation motor evoked potentials (TcMEPs) are widely used for intraoperative spinal cord monitoring. Monitoring of TcMEPs became the gold standard due to their increased sensitivity and the importance of motor function. However, there is no definite alarm point for TcMEPs because previous alarm points were derived from single-institution studies rather than a multicenter study.

We analyzed 48 true-positive cases (that is, decrease in potentials followed by a new neurological motor deficit postoperatively) experienced between 2007 and 2009 from 18 institutions that are part of the monitoring working group of the Japanese Society for Spine Surgery and Related Research and the study group on spinal ligament ossification. Based on this analysis, we designated a decrease in amplitude of 70% or more as the alarm point. The purpose of the current study was to evaluate a new alarm point for TcMEPs in a prospective multicenter study and to demonstrate that a 70% decrease in amplitude represents a more accurate alarm point than those used previously.

Methods

We performed intraoperative spinal cord monitoring using TcMEPs in 959 patients with spinal deformities, OPLL, and spinal cord tumors between 2010 and 2012. There were 360 cases of spinal cord tumor (38%), 317 cases of OPLL (33%), and 282 cases of spinal deformity (29%). We also included 93 patients with intramedullary spinal cord tumors and 114 patients with thoracic OPLL (Fig. 1).

Monitoring of TcMEPs was performed under uniform monitoring conditions at the 18 hospitals belonging to the Spinal Cord Monitoring Working Group of the Japanese Society for Spine Surgery and Related Research and of the study group on spinal ligament ossification. This study was supported by a Japanese Health Labor Sciences research grant.

Total intravenous anesthesia was administered during intraoperative spinal cord monitoring. The drugs administered were propofol (3–4 μg/ml), fentanyl (2 μg/kg), and vecuronium (0.12–0.16 mg/kg). Anesthesia was maintained using propofol (3 μg/ml), fentanyl (1 μg/kg/hr), and vecuronium (0–0.04 mg/kg/hr) and did not exceed 2/4 train of four. The transcranial stimulus conditions comprised 5 train stimuli, a stimulus interval of 2 msec, a stimulus of 300–600 V, a filter of 50–1000 Hz, a recording time of 100 msec, and a total of fewer than 20 stimuli. The stimulator was placed 2 cm anterior and 4 cm lateral to Cz (International 10-20 system) over the cerebral cortex motor area.

The TcMEPs were recorded from the peripheral limbs via needle or disc electrodes and from the anus via plug-type electrodes. The evoked muscles, depending on the site of surgery, were selected from some or all of the deltoid, biceps, triceps, hypothenar, quadriceps femoris, hamstrings, tibialis anterior, gastrocnemius, and sphincter muscles. We measured the amplitudes of TcMEPs by peak-to-peak voltages. The amplitudes prior to the invasive procedures were regarded as control values.

Our alarm point was designated as a decrease in amplitude of 70% or greater. We set the alarm point based on our retrospective analysis of 48 true-positive cases experienced between 2007 and 2009 from 18 institutions belonging to the monitoring working group of the Japanese Society for Spine Surgery and Related Research. The TcMEPs in these cases showed that we could not predict mild postoperative paralysis (1-grade decrease in the manual muscle testing [MMT] grade). However, all cases with moderate-to-severe postoperative paralysis (2- to 5-grade decrease in MMT grade) exhibited a greater than 70% decrease in TcMEP amplitude at the end of surgery (Fig. 2).

As Kim et al. reported, a true-positive case is defined as a TcMEP alert with a persistent decrease in potentials at the end of the operation, followed by the observation of a new neurological motor deficit after the operation. A false-positive case is defined as an alert with a persistent decrease of potentials at the end of the operation and the absence of any new postoperative deficit. A true-negative case is defined as the absence of any TcMEP alert during surgery and no new postoperative deficits. A false-nega-
The true case is defined as the absence of an alert in a patient with a new postoperative motor deficit. A TcMEP alert that normalized after corrective measures in a patient who emerged without new motor deficits was defined as indeterminate (rescue case). Variability of the TcMEPs and the pre- and postoperative motor deficit were analyzed prospectively. Informed consent was obtained from all patients.

**Results**

The TcMEPs yielded 38 true-positive cases, 786 true-negative cases, 78 false-positive cases, and 2 false-negative cases in this study (Fig. 3). The remaining 55 cases were rescue cases. Therefore, the sensitivity was 95%, and the specificity was 91%. The positive predictive value was 32.8%, the negative predictive value was 99.7%, the false-positive rate was 9.0%, and the false-negative rate was 5.0% (Fig. 4). In 55 cases, the TcMEP amplitudes decreased during surgery; however, they recovered at the end of surgery subsequent to steroid injection or release of the scoliosis correction. We regarded these 55 cases as rescue cases; they were excluded from the analysis of monitoring accuracy because without a wakeup test we were not convinced that the temporal decrease in amplitude indicated real motor deficit. The patients in the false-negative cases recovered fully from their transient paralysis.

There were 38 true-positive cases that included 15 patients with thoracic OPLL, 7 patients with extramedullary spinal cord tumor, and 7 patients with intramedullary spinal cord tumor (Fig. 5).

The duration of postoperative paralysis was not associated with the degree of decreased amplitude. Twelve of the 38 true-positive cases lost motor evoked potentials (MEPs) completely at the end of the operations, and the patients recovered their motor function within 1 month. Motor deficits lasting more than 3 months occurred in 9 cases of absent response, 2 cases of amplitude decreased by 80%, and 3 cases of amplitude decreased by 70% (Fig. 6).

Both false-negative cases occurred during surgery for cervical intramedullary spinal cord tumors. One of these patients was paralyzed postoperatively with a 54% decrease in amplitude in the triceps MEPs at the end of surgery. In the other patient, the TcMEP in the tibialis anterior muscle decreased by 52%, and postoperatively the MMT grade in this muscle deteriorated from 4 to 2.

There was one true-positive case in a patient with cervical OPLL; a 75% decrease in amplitude was noted at the end of surgery, and postoperatively the patient’s MMT grade worsened from 4 to 0. Regarding this case, the 80% decrease amplitude criterion was unable to predict neurological deterioration after surgery (Fig. 7).

The accuracy of monitoring using a criterion of a 70% decrease in amplitude was high with a sensitivity of 95% and specificity of 91%.

**Fig. 2.** Retrospective data of 48 cases of postoperative neurological deterioration experienced between 2007 and 2009 from our 18 institutions. All TcMEPs in patients with moderate to severe neurological deterioration decreased more than 70% in amplitude. Thus, we set the alarm point as a greater than 70% decrease in amplitude.

**Fig. 3.** TcMEP monitoring and clinical results with a criterion of a 70% decrease in amplitude. There were 38 true-positive (T.P.) cases and 2 false-negative (F.N.) cases, which were both intramedullary spinal cord tumors. There were 55 indeterminate cases that were excluded from the analysis of monitoring accuracy. F.P. = false positive; T.N. = true negative.

**Fig. 4.** Accuracy of TcMEP monitoring using a criterion of a 70% decrease in amplitude. FNR = false-negative rate; FPR = false-positive rate; NPV = negative predictive value; PPV = positive predictive value.
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Discussion

Warning criteria for TcMEPs are not well established because no previous prospective multicenter study has been published. Most reports have used a criterion of a 50%–80% decrease in amplitude, but some reports used complete loss of response or morphological change. Intraoperative spinal cord monitoring has been used for various spinal diseases. The 70% decrease in amplitude criterion in our study yielded a higher accuracy for neurological deterioration after spinal cord tumor, deformity, and OPLL surgery.

As a historical cohort, Raynor et al. reported a 25-year experience of intraoperative spinal cord monitoring in 12,375 spinal surgeries. They described 386 monitoring alerts and 14 cases of permanent neurological deterioration when they used threshold criterion. Therefore, their study reported more alerts and fewer cases of neurological deterioration than ours (Table 1).

Park et al. reported a 50% amplitude criterion in 29 cervical kyphosis surgeries. The TcMEPs yielded a sensitivity of 75% and a specificity of 84%. Lee et al. reported a 60% amplitude criterion in 1445 anterior cervical surgeries. There were 267 TcMEP alerts (18.4%) and only 2 neurological deficits. We thought that a criterion of a 50%–60% decrease in amplitude provided an excess of alarms and reduced specificity.

Langeloo et al. reported on 145 patients with spinal deformity who underwent corrective surgery with TcMEP monitoring. The alarm point was designated as a response amplitude decrease of more than 80% that resulted in 16 TcMEP alerts and only 5 neurological deficits, a sensitivity of 100%, and a specificity of 91%. They reported a reduced incidence in postoperative neurological deterioration. In our study, we observed 171 TcMEP alerts and 40 cases of neurological deterioration. One patient with cervical OPLL exhibited a postoperative decrease in TcMEP amplitude of 75% with severe neurological deterioration postoperatively (MMT grade from 4 to 0). In our retrospective study from 2007 to 2009 we also observed 4 patients who exhibited a 70%–80% decrease in TcMEP amplitude and who had moderate postoperative neurological deterioration. These cases suggested that the 80% amplitude criteria exhibited reduced sensitivity compared with the 70% amplitude criterion. These cases supported high validity of the 70% amplitude criterion. The criterion of a 70% decrease in amplitude was useful for predicting neurological injury, and we could avoid neurological complications based on TcMEPs.

Sala et al. reported that TcMEP disappearance was a reason to modify intramedullary spinal cord tumor surgery, but a 50% D-wave amplitude decrease was the major indication to stop surgery. We observed 16 patients with neurological deterioration of more than 2 grades in MMT in whom TcMEPs disappeared entirely. Our study suggests that a complete loss of response indicates mild to severe paralysis; thus, loss of response is too late to alarm. There were 78 false-positive cases in our study. According to other studies, the definition of false-positive was based on neurological “events.” However, our definition of false-positive was based on neurological de-
TABLE 1: Literature review of TcMEP alarm points*

<table>
<thead>
<tr>
<th>Authors &amp; Year</th>
<th>Diagnosis</th>
<th>TcMEP Criterion</th>
<th>Other Modality</th>
<th>No. of Cases</th>
<th>Monitoring Alerts</th>
<th>Neurological Deterioration</th>
<th>Precision (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pelosi et al., 2002</td>
<td>deformity</td>
<td>50%</td>
<td>SSEP</td>
<td>126</td>
<td>16</td>
<td>1</td>
<td>6</td>
</tr>
<tr>
<td>Langeloo et al., 2003</td>
<td>deformity</td>
<td>80%</td>
<td>SSEP</td>
<td>132</td>
<td>16</td>
<td>3</td>
<td>19</td>
</tr>
<tr>
<td>Quiñones-Hinojosa et al., 2005</td>
<td>SCT</td>
<td>waveform</td>
<td>28</td>
<td>13</td>
<td>12</td>
<td>92</td>
<td></td>
</tr>
<tr>
<td>Lee et al., 2006</td>
<td>cervical pathology</td>
<td>60%, 10% latency</td>
<td>SSEP</td>
<td>1445</td>
<td>67</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>Kim et al., 2007</td>
<td>cervical pathology</td>
<td>80%</td>
<td>SSEP</td>
<td>52</td>
<td>6</td>
<td>1</td>
<td>17</td>
</tr>
<tr>
<td>Sutter et al., 2007</td>
<td>SCT</td>
<td>50%, 10% latency</td>
<td>109</td>
<td>25</td>
<td>4</td>
<td>16</td>
<td></td>
</tr>
<tr>
<td>Park et al., 2011</td>
<td>deformity</td>
<td>50%, 10% latency</td>
<td>SSEP, EMG</td>
<td>29</td>
<td>7</td>
<td>4</td>
<td>57</td>
</tr>
<tr>
<td>Ito et al., 2012</td>
<td>spinal pathology</td>
<td>waveform</td>
<td>295</td>
<td>67</td>
<td>8</td>
<td>12</td>
<td></td>
</tr>
<tr>
<td>Raynor et al., 2013</td>
<td>spinal pathology</td>
<td>threshold</td>
<td>SSEP, EMG</td>
<td>12,375</td>
<td>386</td>
<td>14</td>
<td>4</td>
</tr>
<tr>
<td>present study</td>
<td>OPLL, deformity, SCT</td>
<td>70%</td>
<td>959</td>
<td>116</td>
<td>40</td>
<td>35</td>
<td></td>
</tr>
</tbody>
</table>

* EMG = electromyography; SCT = spinal cord tumor; SSEP = somatosensory evoked potential.

Conclusions

The new criterion of a 70% decrease in amplitude of TcMEPs provided increased sensitivity (95%) and specificity (91%) for intraoperative spinal cord monitoring. Thus, a 70% decrease in amplitude was the ideal TcMEP alarm point, except in cases of intramedullary spinal cord tumor. We recommend this alarm point for routine spinal cord monitoring, particularly for surgery treating spinal deformities, extramedullary spinal cord tumors, and OPLLs.

Disclosure

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Author contributions to the study and manuscript preparation include the following. Conception and design: Matsuyama. Acquisition of data: Kobayashi, Kawabata, Ando, Kanchiku, Saito, Takahashi, Ito, Muramoto, Fujiwara, Kida, Yamada, Wada, Yamamoto. Analysis and interpretation of data: Kobayashi, Shinomiya, Kawabata, Ando, Kanchiku, Saito, Takahashi, Ito, Muramoto, Fujiwara, Kida, Yamada, Wada, Yamamoto. Drafting the article: Kobayashi. Critically revising the article: all authors. Reviewed submitted version of manuscript: all authors. Approved the final version of the manuscript on behalf of all authors: Kobayashi. Study supervision: Matsuyama, Shinomiya, Satomi, Tani.

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