Multimodal neurophysiological monitoring is commonly used in complex spine surgeries for prevention of intraoperative neurological injury. In 1980, Merton and Morton introduced a novel technique for intraoperative neurophysiological monitoring of spinal cord integrity by using MEP monitoring, which has since become the standard for intraoperative monitoring. This was initially accomplished by stimulating the motor cortex transcranially, and recording the subsequent evoked action potentials in peripheral muscles. Monitoring of the motor tracts allowed real-time assessment of the integrity of the descending pyramidal tracts. Importantly, monitoring of the motor pathways included portions of the spinal cord supplied by the anterior spinal artery. Compromise of this vascular distribution largely spares the dorsal columns, which is the dominant substrate for somatosensory evoked potential monitoring.

Variations of the transcranial method of stimulation followed, including stimulation of the spinal cord, skull, hard palate, and exposed motor cortex. Transcranial magnetic stimulation of MEPs was successfully accomplished as well, but it is an impractical method, given the complex electromagnetic environment within the operating room and the ease of electrical stimulation.

Early attempts at MEP monitoring encountered similar difficulties, with signal suppression due to anesthesia. Inghilleri et al. first reported improved monitoring with paired stimulation, which is attributed to effective accumulation of excitatory postsynaptic potentials at the level of the anterior horn motor neurons. Application of a short train of stimulation, spaced 2-5 msec apart, was found to improve greatly the reliability of MEP monitoring. Later, the application of a 2- to 5-second tetanic stimulation to the peripheral muscles ~ 1-5 seconds prior to TcMEP stimulation could effectively augment MEP monitoring.

Presently, TcMEPs are commonly used in complex spinal operations, including tumor and deformity surgery. Given that neurophysiological monitoring can be significantly influenced by anesthesia, awareness of how various anesthetic agents can impact TcMEPs is essential.

Methods
An extensive search of the US National Library of Medicine database was performed using the terms “anesthesia,” “neurophysiology,” “electrophysiology,” “motor evoked potential,” “monitoring,” and “spine surgery.”
Retrieved articles were screened for human patients undergoing spine surgery in which electric TcMEP monitoring was used. Case reports and small studies of < 5 patients were excluded. From among the 50 articles initially identified, we selected 20 articles in which the effect of anesthetic agents on TcMEP monitoring was studied.

### TABLE 1: Literature review of clinical studies reporting the effect of anesthetic regimens used in spine surgeries involving intraoperative MEP monitoring

<table>
<thead>
<tr>
<th>Authors &amp; Year</th>
<th>No. of Patients</th>
<th>Anesthetic Agents Used</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Zentner et al., 1989</td>
<td>15</td>
<td>nitrous oxide, fentanyl, flunitrazepam, thiopental</td>
<td>nitrous oxide decreased electric TcMEP amplitudes, whereas fentanyl, flunitrazepam, &amp; thiopental had only a minor effect on TcMEP</td>
</tr>
<tr>
<td>Calancie et al., 1991</td>
<td>8</td>
<td>isoflurane</td>
<td>addition of isoflurane resulted in marked attenuation of electric TcMEP responses</td>
</tr>
<tr>
<td>Jellinek et al., 1991</td>
<td>34</td>
<td>propofol</td>
<td>although propofol anesthesia caused reduction in magnetic TcMEP amplitude, intraop monitoring was sensitive to disturbance in motor pathways</td>
</tr>
<tr>
<td>Jellinek et al., 1991</td>
<td>34</td>
<td>nitrous oxide &amp; propofol</td>
<td>w/ concentrations &lt; 50%, nitrous oxide can be used w/o significant negative effect on electric TcMEPs in patients under propofol anesthesia</td>
</tr>
<tr>
<td>Kalkman et al., 1992</td>
<td>11</td>
<td>vecuronium</td>
<td>electric TcMEP monitoring is possible w/ partial neuromuscular blockade</td>
</tr>
<tr>
<td>Taniguchi et al., 1993</td>
<td>77</td>
<td>propofol, etomidate, methohexital, or thiopental</td>
<td>all 4 intravenous anesthetic agents shown to have negative influence on magnetic TcMEP monitoring</td>
</tr>
<tr>
<td>Woodforth et al., 1996</td>
<td>6</td>
<td>isoflurane &amp; nitrous oxide</td>
<td>satisfactory electric TcMEPs could be obtained w/ nitrous oxide &amp; isoflurane (0.1%-0 for 10 min); isoflurane concentrations &gt; 0.1% resulted in loss of responses</td>
</tr>
<tr>
<td>Ubags et al., 1997</td>
<td>18</td>
<td>etomidate or ketamine + sufentanil + nitrous oxide</td>
<td>etomidate or ketamine can be used to supplement nitrous oxide/opioid anesthesia w/o significant impact on electric TcMEP monitoring</td>
</tr>
<tr>
<td>Ubags et al., 1998</td>
<td>10</td>
<td>isoflurane</td>
<td>isoflurane significantly depresses single-stimulus electric TcMEPs, but multi-stimulus TcMEPs can allow monitoring up to 1 MAC of isoflurane w/ nitrous oxide/opioid anesthesia</td>
</tr>
<tr>
<td>Kawaguchi et al., 2000</td>
<td>58</td>
<td>nitrous oxide–fentanyl–ketamine w/ or w/o low-dose (1–3 mg/kg/hr) propofol</td>
<td>propofol negatively affects single-stimulus electric TcMEPs, but train of stimuli for TcMEPs allows use of low-dose propofol to supplement ketamine-based anesthesia</td>
</tr>
<tr>
<td>Pelosi et al., 2001</td>
<td>50</td>
<td>propofol &amp; nitrous oxide vs isoflurane &amp; nitrous oxide</td>
<td>multipulse electric TcMEP monitoring possible in 97% of spinal ops w/ propofol, nitrous oxide, &amp; opioid anesthesia; only 61% could be monitored w/ isoflurane, nitrous, &amp; opioid anesthesia</td>
</tr>
<tr>
<td>Scheufler &amp; Zentner, 2002</td>
<td>40</td>
<td>alfentanil, sufentanil, fentanyl, remifentanil, thiopental, midazolam, etomidate, ketamine, &amp; propofol</td>
<td>TIVA using remifentanil &amp; midazolam (or propofol) allows satisfactory monitoring of magnetic TcMEPs; etomidate &amp; midazolam had minimal effect on TcMEPs; ketamine had a suppressive influence at high doses</td>
</tr>
<tr>
<td>Nathan et al., 2003</td>
<td>15</td>
<td>propofol</td>
<td>multipulse electric TcMEPs were reduced in a dose-dependent manner, although latencies were unchanged w/ propofol; combining propofol w/ remifentanil can allow adequate monitoring</td>
</tr>
<tr>
<td>Chen, 2004</td>
<td>35</td>
<td>isoflurane vs propofol</td>
<td>intravenous anesthesia w/ propofol allowed adequate monitoring in all patients by using multipulse electric TcMEPs; only 58.8% of patients could be monitored when isoflurane anesthesia was used</td>
</tr>
<tr>
<td>Lo et al., 2004</td>
<td>10</td>
<td>desflurane</td>
<td>combination of nitrous oxide &amp; desflurane (0.5% maximum alveolar concentration) allowed adequate monitoring using multipulse electric TcMEPs</td>
</tr>
<tr>
<td>Lo et al., 2006</td>
<td>20</td>
<td>desflurane vs TIVA</td>
<td>both anesthetic regimens (desflurane w/ nitrous oxide &amp; TIVA w/ propofol) allowed adequate monitoring w/ multipulse electric TcMEPs</td>
</tr>
<tr>
<td>Zaarour et al., 2007</td>
<td>34</td>
<td>ketamine added to TIVA (propofol &amp; remifentanil)</td>
<td>addition of low-dose ketamine did not limit the voltage necessary to obtain maximal amplitude responses w/ electric TcMEPs</td>
</tr>
<tr>
<td>Anschel et al., 2008</td>
<td>18</td>
<td>dexmedetomidine added to TIVA</td>
<td>dexmedetomidine can be used as an adjunct to TIVA w/o significantly impacting TcMEP monitoring</td>
</tr>
<tr>
<td>Tobias et al., 2008</td>
<td>9</td>
<td>dexmedetomidine added to TIVA (propofol &amp; remifentanil)</td>
<td>w/ adjustment of propofol dosing, dexmedetomidine can be added as a supplement to the anesthetic regimen w/o significantly influencing electric TcMEP monitoring</td>
</tr>
<tr>
<td>Hayashi et al., 2009</td>
<td>35</td>
<td>sevoflurane</td>
<td>sevoflurane suppressed TcMEP monitoring; no significant difference between conventional &amp; posttetanic MEP monitoring observed</td>
</tr>
</tbody>
</table>
Anesthesia and transcranial motor evoked potentials

TABLE 2: Key points regarding the impact of anesthesia on TcMEP monitoring

<table>
<thead>
<tr>
<th>Inhalational halogenated anesthetics &amp; nitrous oxide lead to a dose-dependent reduction in MEP signal amplitude, limiting the ability to detect significant neurological changes</th>
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<tbody>
<tr>
<td>Use of TIVA can minimize the need for halogenated anesthetics</td>
</tr>
<tr>
<td>TIVA regimens can include a combination of propofol, synthetic narcotics, &amp; N-methyl-D-aspartate receptor antagonists (that is, ketamine)</td>
</tr>
<tr>
<td>Neuromuscular blockade &amp; hypothermia also suppress MEP recording</td>
</tr>
<tr>
<td>Opioids have minimal impact on MEP recording</td>
</tr>
<tr>
<td>Regardless of regimen used, it is crucial to maintain a stable concentration of the inhalational or intravenous anesthetic, because sudden changes in dosage can cause MEP changes, making interpretation difficult</td>
</tr>
</tbody>
</table>

Results and Discussion

Transcranial MEP recording, when used as a part of multimodality intraoperative neurophysiological monitoring, is exquisitely sensitive in recognizing intraoperative nervous injury, both by mechanical and by ischemic mechanisms. However, MEP recordings are also known to be affected by a number of anesthetic agents, due to the inhibitory effect of inhalational anesthetics at the cortical axon synapses and spinal anterior horn cells. At the time of Merton and Morton’s experiments, halogenated anesthetics and nitrous oxide were commonly used in spine surgeries. The tendency of these anesthetics to depress motor neuron activity was quickly discovered, and intravenous anesthesia was introduced, initially using fentanyl and propofol, to mitigate this effect.

The successful performance of intraoperative neurophysiological monitoring is dependent on careful maintenance of a steady and consistent electrophysiological baseline. The anesthetic regimens used in spine surgeries involving the use of intraoperative MEP monitoring have since been studied in great detail. Relevant clinical studies are listed in Table 1. All volatile halogenated anesthetics, as well as nitrous oxide, produce a dose-dependent reduction in MEP signal amplitude. Because the signal amplitudes of MEP recordings are already quite small, the effect of these inhalational agents can limit the practitioner’s ability to detect significant changes intraoperatively. A number of studies have shown that with partial neuromuscular blockade, effective monitoring could still be performed at 0.5 MAC, with more variability at 1.0 MAC. With other, less disruptive options available, inhalational agents are generally to be avoided in cases requiring neurophysiological monitoring.

With the relative ease of TIVA administration, the need for inhalational anesthetics can be minimized. Various combinations of intravenous anesthetic regimens have been described and tested intraoperatively. Propofol, synthetic narcotics, and N-methyl-D-aspartate receptor antagonists have been used successfully in sizable series of spine operations, as detailed in Table 1. Although propofol does demonstrate a dose-dependent reduction in MEP amplitude without effect on latency, it has repeatedly been shown to produce a more stable neurophysiological environment for monitoring, when compared with inhalational anesthetics.

Opioids have shown minimal influence on MEP recording, and administered as a continuous infusion, are an invaluable part of an anesthetic regimen for spine surgery requiring neurophysiological monitoring. More recently, interest has been shown in using ketamine and dexmedetomidine as part of a TIVA regimen. Ketamine is known to enhance the monitoring of evoked potentials, and has demonstrated its utility in a number of studies. Dexmedetomidine has been used as a supplement to TIVA to reduce the dose of propofol, without evidence of detriment. Neuromuscular blockade is known to suppress MEP signal recording. Partial paralysis has been used on rare occasions, but is generally too unpredictable to use regularly.

Electric conduction increases in velocity with temperature, and the same principle appears to apply in MEP monitoring. Hypothermia is thought to decrease the reliability of MEP monitoring, demonstrating an increase in stimulation threshold with decreasing temperatures. Similarly, latency is reduced and conduction velocity increased with hyperthermia, although MEPs deteriorate above 42°C (Table 2).

Conclusions

Overall, intraoperative neurophysiological monitoring has been shown to offer excellent reliability in assessing iatrogenic neurological injury. Selection of the appropriate anesthetic regimen can help to optimize the data recorded. Regardless of the regimen used, it is of utmost importance to maintain a stable concentration of inhalational or intravenous anesthetic. Although improvements in monitoring technology have compensated for inherently low signal amplitudes that are made more difficult by the nature of anesthesia, sudden changes in dose can induce MEP changes, making interpretation impossible.

Disclaimer

The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

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