Effects of Anesthetic Agents and Physiologic Changes on Intraoperative Motor Evoked Potentials

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Abstract: Motor evoked potentials (MEPs) have shown promise as a valuable tool for monitoring intraoperative motor tract function and reducing postoperative plegia. MEP monitoring has been reported to contribute to deficit prevention during resection of tumors adjacent to motor structures in the cerebral cortex and spine, and in detecting spinal ischemia during thoracic aortic reconstruction. Many commonly used anesthetic agents have long been known to depress MEP responses and reduce MEP specificity for motor injury detection. Although new stimulation techniques have broadened the spectrum of anesthetics that can be used during MEP monitoring, certain agents continue to have dose-dependent effects on MEP reliability. Understanding the effects of anesthetic agents and physiologic alterations on MEPs is imperative to increasing the acceptance and application of this technique in the prevention of intraoperative motor tract injury. This review is intended as an overview of the effects of anesthetics and physiology on the reproducibility of intraoperative myogenic MEP responses, rather than an analysis of the sensitivity and specificity of this monitoring method in the prevention of motor injury.

Key Words: intraoperative monitoring, motor evoked potentials, anesthetic agents, neuromuscular blockade, physiologic effects

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MOTOR EVOKED POTENTIALS

MEPs are elicited by initiating a depolarizing action potential in the pyramidal cell axons via a current applied directly or transcranially to the cerebral cortex or spinal cord. Transcranial stimulation can be achieved with high-voltage, short-duration electrical stimulators, or magnetic field induction at the level of the scalp. Either stimulus technique can be applied to multiple areas of the proximal motor structures to generate responses, including the motor cortex, the pyramidal decussation at the brain stem, and the proximal spinal tracts.

MEPs can be recorded from multiple points along the motor structures as the action potential initiated in the motor cortex descends through the corticospinal tract to the alpha motor neuron and the muscle.

Spinal D-Waves

Responses recorded from the spinal tracts by epidural electrodes consist of a direct, or D-wave, and a series of indirect, or I-waves (Fig. 1). The short-latency D-wave is the result of direct activation of the pyramidal cell axon, without the delay of an intervening synapse. The lack of synaptic transmission makes D-wave amplitudes more stable during general anesthesia and thus a more reliable monitor of motor tract function than I-waves. Spinal D-wave amplitudes demonstrate much less variability than responses recorded from the muscle, with only a 10% variability in repeated responses in anesthetized patients. D-wave amplitudes reflect the number of corticospinal neurons activated. A 50% reduction in D-wave amplitudes correlates with postoperative motor weakness. Larger-amplitude changes have been found to predict a more profound neurologic deficit and a lower chance for functional recovery.

Neurogenic MEPs

Neurogenic MEPs (NMEPs) are responses recorded from the peripheral nerve following stimulation of the spinal cord (see Fig. 1). Although NMEPs are relatively resistant to anesthetic depression, the spinal stimulation used to elicit the responses activates both orthodromic motor and antidromic sensory pathways, making NMEPs nonspecific for motor function. Collision studies in human subjects suggest that the responses may be purely sensory, with motor responses due only to sensory and motor connections at the spinal level. Recent reports of unchanged intraoperative NMEPs and somatosensory evoked potentials (SSEPs) in two patients with postoperative motor deficits confirm a mainly sensory contribution.

Myogenic MEPs

Myogenic potentials are large (1–25 mV), biphase responses recorded over the muscle belly (see Fig. 1). Compound muscle action potentials (CMAPs) are generated by the...
Volatile Anesthetics

Halogenated inhalational agents cause significant dose-dependent depression of myogenic response amplitudes and can increase monitoring failure rates at clinically relevant doses (Table 1). Volatile agents inhibit the pyramidal activation of spinal motor neurons at the level of the ventral horn. Spinal volleyes created by single-pulse transcranial stimuli are inadequate to overcome the suppressive effect of even a low-dose inhalational agent (0.25–0.5 MAC). Volatile suppression can be partially overcome by using higher-intensity stimuli and multi-pulse stimulation. Stimulus trains of 3 to 5 pulses improve CMAP amplitudes (mean amplitudes 172 μV) and monitoring success under isoflurane concentrations up to 0.5 MAC (Fig. 2). However, as end-tidal concentrations increase beyond 0.5 MAC, a percentage of subjects lose myogenic responses despite the use of multi-pulse stimuli. Concentrations of 0.75 and 1 MAC isoflurane reportedly produce adequate CMAP responses in only 61% and 8% of patients, respectively, after multi-pulse transcranial electrical stimulation. Dual-pulse electrical stimuli generate CMAP responses in only 55% of patients at 0.5 MAC sevoflurane and 10% at 0.75 MAC. Other volatile agents show similar depressive effects.

Direct stimulation of the motor cortex following craniotomy improves myogenic MEP acquisition over transcranial stimulation in the presence of volatile anesthetics. CMAP responses can be seen at 0.75 to 1.5 MAC isoflurane and sevoflurane following direct motor cortical stimulation.

Volatile agents have much less effect on transcranially elicited spinal D-wave potentials than on myogenic responses. While the transsynaptically generated I-waves show 50% depression at 1 MAC of volatile agent, little change occurs in the D-wave amplitude.

Nitrous Oxide

Nitrous oxide (N₂O) appears to be less suppressive than other inhaled agents and can be used in moderate doses to supplement other agents during myogenic MEP monitoring. Multi-pulse stimulus techniques have been shown to partially reverse the N₂O-induced amplitude depression and response variability previously reported during single-pulse stimulation. The addition of up to 50% N₂O to less suppressive anesthetic regimens such as opioid, ketamine, or low-dose propofol infusions (20–50 μg/kg/min) does not cause significant myogenic response amplitude depression when multi-pulse stimuli are applied transcranially. Reversal of amplitude suppression caused by higher doses of N₂O (60–70%) is less reliable. A 50% to 70% reduction in CMAP amplitudes occurs with addition of 60% N₂O to an opioid and low-dose propofol (0.5–1 μg/mL) anesthetic despite a 6-pulse stimulus application. However, adequate (median 450 μV) and reproducible
TABLE 1. Reported Effects of Anesthetic Agents on MEP Response Amplitudes and Monitoring Success During Various Stimulus Paradigms

<table>
<thead>
<tr>
<th>Agent</th>
<th>Type of Stimulus</th>
<th>Stimulus Paradigm</th>
<th>Median Amplitude (µV)</th>
<th>Amplitude (%) of Baseline</th>
<th>Patients With Responses (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>50% N₂O</td>
<td>TcE</td>
<td>1 pulse (92) φ</td>
<td>401</td>
<td>98</td>
<td>100</td>
</tr>
<tr>
<td></td>
<td>TcE</td>
<td>2 pulse (37) φ (38) ★ *(93) φ#</td>
<td>1,031,629 ± 140</td>
<td>55</td>
<td>100</td>
</tr>
<tr>
<td></td>
<td>TcM</td>
<td>1 pulse (64) # i</td>
<td>192</td>
<td>55</td>
<td>55</td>
</tr>
<tr>
<td>60% N₂O</td>
<td>TcE</td>
<td>6 pulse (39) φ ★</td>
<td>450</td>
<td>100</td>
<td></td>
</tr>
<tr>
<td>Isoflurane 0.16 MAC</td>
<td>TcE</td>
<td>3 pulse (25) φ ⋆</td>
<td>441</td>
<td>61</td>
<td>100</td>
</tr>
<tr>
<td></td>
<td>TcE</td>
<td>5 pulse (25) φ ⋆</td>
<td>560</td>
<td>74</td>
<td>100</td>
</tr>
<tr>
<td>Isoflurane 0.3 MAC</td>
<td>TcE</td>
<td>3 pulse (25) φ ⋆</td>
<td>293</td>
<td>40</td>
<td>100</td>
</tr>
<tr>
<td></td>
<td>TcE</td>
<td>5 pulse (25) φ ⋆</td>
<td>337</td>
<td>44</td>
<td>100</td>
</tr>
<tr>
<td>Isoflurane 0.5 MAC</td>
<td>TcE</td>
<td>3 pulse (25) φ ⋆</td>
<td>172</td>
<td>24</td>
<td>90</td>
</tr>
<tr>
<td></td>
<td>TcE</td>
<td>5 pulse (25) φ ⋆</td>
<td>184</td>
<td>24</td>
<td>90</td>
</tr>
<tr>
<td>Isoflurane 0.75 to 1 MAC</td>
<td>TcE</td>
<td>4 pulse (26) φ ★</td>
<td>92</td>
<td>100</td>
<td>43</td>
</tr>
<tr>
<td></td>
<td>TcE</td>
<td>5 pulse (27) φ ★</td>
<td>8</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sevoflurane 0.25 MAC</td>
<td>TcE</td>
<td>2 pulse (28) φ ⋆</td>
<td>37</td>
<td>27</td>
<td>85</td>
</tr>
<tr>
<td>Sevoflurane 0.5 MAC</td>
<td>TcE</td>
<td>2 pulse (28) φ ⋆</td>
<td>10</td>
<td>7</td>
<td>55</td>
</tr>
<tr>
<td>Sevoflurane 0.75 MAC</td>
<td>TcE</td>
<td>2 pulse (28) φ ⋆</td>
<td>0</td>
<td>0</td>
<td>10</td>
</tr>
<tr>
<td>Sevoflurane 1.0 MAC</td>
<td>TcE</td>
<td>2 pulse (28) φ #</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Propofol 20–25 µg/kg/min</td>
<td>TcE</td>
<td>2 pulse (38) φ *</td>
<td>638</td>
<td>85</td>
<td>100</td>
</tr>
<tr>
<td></td>
<td>TcE</td>
<td>6 pulse (48) φ #</td>
<td>813</td>
<td>100</td>
<td></td>
</tr>
<tr>
<td></td>
<td>TcM</td>
<td>5 pulse (61) # i</td>
<td>2503</td>
<td>86</td>
<td>100</td>
</tr>
<tr>
<td>25–50 µg/kg/min</td>
<td>TcE</td>
<td>2 pulse (38) φ #</td>
<td>519</td>
<td>69</td>
<td>100</td>
</tr>
<tr>
<td></td>
<td>TcE</td>
<td>6 pulse (48) φ #</td>
<td>526,128</td>
<td>28</td>
<td></td>
</tr>
<tr>
<td></td>
<td>TcM</td>
<td>5 pulse (51) # i</td>
<td>822</td>
<td>28</td>
<td>92–100</td>
</tr>
<tr>
<td>50–75 µg/kg/min</td>
<td>TcE</td>
<td>5 pulse (49) φ #</td>
<td>23</td>
<td>23</td>
<td>80</td>
</tr>
<tr>
<td>75–100 µg/kg/min</td>
<td>TcE</td>
<td>2 pulse (37) φ</td>
<td>655</td>
<td>63</td>
<td>83</td>
</tr>
<tr>
<td></td>
<td>TcE</td>
<td>5 pulse (49) φ #</td>
<td>131,035 ± 125</td>
<td>13</td>
<td>60188</td>
</tr>
<tr>
<td></td>
<td>TcE</td>
<td>5 pulse (51) &quot;&quot;&quot;</td>
<td>560</td>
<td>19</td>
<td></td>
</tr>
<tr>
<td>&gt;100 µg/kg/min</td>
<td>TcE</td>
<td>4 pulse (26) φ #</td>
<td>134</td>
<td>96</td>
<td></td>
</tr>
<tr>
<td></td>
<td>TcM</td>
<td>5 pulse (51) &quot;&quot;&quot;</td>
<td>355</td>
<td>12</td>
<td></td>
</tr>
<tr>
<td>Ketamine 1 mg/kg/hr</td>
<td>TcE</td>
<td>3 pulse (49) φ #</td>
<td>60 &quot;</td>
<td>91 &quot;</td>
<td></td>
</tr>
<tr>
<td></td>
<td>TcM</td>
<td>5 pulse (60) φ #</td>
<td>400</td>
<td>100</td>
<td></td>
</tr>
<tr>
<td>Sufentanil 0.5 mcg/kg/hr</td>
<td>TcE</td>
<td>1 pulse (92) φ #</td>
<td>401</td>
<td>100</td>
<td></td>
</tr>
<tr>
<td></td>
<td>TcE</td>
<td>2 pulse (50) φ #</td>
<td>311,110,31</td>
<td>100</td>
<td></td>
</tr>
<tr>
<td></td>
<td>TcE</td>
<td>3 pulse (25) φ #</td>
<td>287</td>
<td>100</td>
<td></td>
</tr>
</tbody>
</table>

Responses were obtained despite the moderate reduction in response size.35 Recent animal data suggest that the suppressive effects of other anesthetic agents may have a synergistic effect on N₂O-induced MEP amplitude depression. The authors found that CMAP amplitude reduction caused by 30% to 70% N₂O could be fully reversed by 5-pulse train stimuli when combined with agents known to have minimal effects on CMAP response amplitudes, such as ketamine/opioid infusions. However, N₂O-induced suppression could not be reversed even with multi-pulse stimulation when combined with propofol at serum concentrations of 1.6 µg/mL.40

N₂O has little effect on the D-wave component of the cortical spinal volley, although some depression of the I-wave amplitude is seen. Several authors have reliably recorded spinal cord evoked potentials with concentrations of N₂O up to 70%.14,41

Barbiturates

Thiopental causes a dose-dependent decrease in CMAP amplitudes and an increase in stimulation thresholds. Complete loss of CMAP responses occurs with thiopental doses of 4 to 9 mg/kg.42–44

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TABLE 1. (continued) Reported Effects of Anesthetic Agents on MEP Response Amplitudes and Monitoring Success During Various Stimulus Paradigms

<table>
<thead>
<tr>
<th>Agent</th>
<th>Type of Stimulus</th>
<th>Stimulus Paradigm</th>
<th>Median Amplitude (µV)</th>
<th>Amplitude (%) of Baseline</th>
<th>Patients With Responses (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Remifentanil 9 ng/ml*</td>
<td>TC</td>
<td>2 pulse (61)</td>
<td>750±1</td>
<td>40</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>4 pulse (61)</td>
<td>1500±1</td>
<td>50</td>
<td></td>
</tr>
<tr>
<td>Neuromuscular blockade T1</td>
<td>TC</td>
<td>2 pulse (65)†</td>
<td>105</td>
<td>180</td>
<td>100</td>
</tr>
<tr>
<td>45–55% baseline</td>
<td></td>
<td>6 pulse (65)†</td>
<td>948</td>
<td>97</td>
<td>100</td>
</tr>
<tr>
<td>T1 15–20% baseline</td>
<td>TC</td>
<td>1 pulse (53)‡</td>
<td>600</td>
<td>56</td>
<td>95</td>
</tr>
<tr>
<td>T1 5–15% baseline</td>
<td>TC</td>
<td>2 pulse (65)†</td>
<td>38</td>
<td>66</td>
<td>100</td>
</tr>
<tr>
<td></td>
<td></td>
<td>6 pulse (65)†</td>
<td>272</td>
<td>28</td>
<td>100</td>
</tr>
<tr>
<td>Midazolam 0.1 mg/kg/hr</td>
<td>TC</td>
<td>1 pulse (64)§</td>
<td>525</td>
<td>198</td>
<td>87†</td>
</tr>
<tr>
<td>Etomidate 5–10 mcg/kg/min</td>
<td>TC</td>
<td>1 pulse (64)¥</td>
<td>229</td>
<td>93</td>
<td>77‡</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1 pulse (53)§</td>
<td>1062</td>
<td>100‡</td>
<td></td>
</tr>
</tbody>
</table>

*Partial neuromuscular blockade T1 of TOF at 40–50% of control.
†Partial neuromuscular blockade T1% of TOF at 15–25% of control.
§Partial neuromuscular blockade T1 and T2 visible.
◆ Narcotic bolus.
+N2O.
Midazolam 0.1 mg/kg/hr.
#Ketamine.
€Propofol 0.5–1.0 µg/mL.
£Propofol 40–50 mcg/kg/min (1 µg/mL).
†Median size of CMAP amplitude after addition of drug.
‡% change in CMAP amplitude after addition of drug.
§N2O added to patients with four different TIVA regimens including alfentanil-etomidate, alfentanil-propofol, propofol-ketamine, midazolam-ketamine.
¥Success of bilateral myogenic recording, unilateral recording obtained in 61%.
Approximate infusion rate to produce reported serum propofol concentration of 0.7–1 µg/mL.
Approximate infusion rate to produce reported propofol serum concentration of 1.4–2 µg/mL.
Reported serum propofol concentration of 5 µg/mL.
*Study group included patients with preoperative motor dysfunction.
Infusion rate to induce loss of consciousness in 50% of patients.
Numbers are approximate/extrapolated from box plot data.

Methohexital infusion maintains better monitoring conditions than thiopental, although some dose-dependent depression of CMAP does occur. Single-pulse, myogenic responses were lost in 60% to 80% of patients after infusion of subanesthetic doses of thiopental compared with 43% of patients anesthetized with induction doses of methohexital. Using single-train stimulation, Watt et al. reported adequate tcM MEP production in seven of seven patients receiving methohexital (100 mcg/kg/min)/alphentanil, ketamine (14–20 mcg/kg/min), and low-dose N2O (25%). The same authors later noted similar recording success and faster emergence times with the omission of ketamine and the substitution of remifentanil for alfentanil. Under single-pulse stimulation, anesthetic maintenance with methohexital provided better monitoring conditions than propofol infusion and comparable conditions to etomidate infusion. Use of multi-pulse stimuli in patients under methohexital anesthesia has not been reported.

Propofol

Despite its depressive effect on the motor system, the rapid metabolism and titratability of propofol have made it a popular anesthetic for use during evoked potential monitoring in cases requiring early postoperative emergence for neurologic examination. Thus, much energy has been spent on developing techniques that allow myogenic MEP monitoring under propofol infusion. Propofol suppresses activation of the alpha motor neuron at the level of the spinal gray matter. As with other agents, multi-pulse stimulation techniques can improve response amplitudes and monitoring success under propofol anesthesia. The dose–response curve of propofol CMAP suppression is difficult to ascertain due to variations in agent combination and muscle relaxation used by various authors. There does appear to be a limit to serum propofol levels above which myogenic MEP monitoring is compromised despite multi-pulse stimulus techniques. When serum propofol levels are maintained at or below 1 µg/mL (20–25 µg/kg/min)
and supplemented by opioid/50% N₂O, transcranial electric stimulation applied in 2 to 6 pulses produced CMAP responses in 100% of patients (median amplitudes 600-900 µV).³⁸,³⁹,⁴⁸ Serum propofol concentrations between 1 to 2 µg/mL (25-50 µg/kg/min) caused a 30% to 60% reduction in CMAP amplitude despite multi-stimulus techniques, although response acquisition and reproducibility were well maintained.⁴⁸ Above 3 µg/mL (75-100 µg/kg/min), greater variability in response depression has been reported, ranging from 33% to 83%.²⁷,⁴⁹ Response acquisition was adequate in only 60% to 88% of patients above this serum concentration.²⁷,⁴⁹,⁵⁰

Scheufler and Zentner⁵¹ recently used transcranial magnetic stimulation to more clearly demonstrate the effects of propofol used as a single agent. At plasma propofol levels of 3 mcg/mL (75-100 µg/kg/min), increasing stimuli rates from 2 to 4 pulses more than doubled CMAP amplitudes, generating mean waveforms of 517 µV. At higher serum propofol levels (≥5 µg/mL [≥100 µg/kg/min]), a greater amplitude depression was seen despite increasing impulse numbers, although CMAP responses did remain recordable with mean amplitudes of 264 µV.⁵¹

Etomidate

Etomidate produces minimal suppression of myogenic transcranial MEPS when compared with barbiturates or propofol. Injection of an induction dose of etomidate (0.3 mg/kg) does cause CMAP amplitude depression to 35% of baseline without changes in latency.⁴³,⁴⁴ The depressive effect, however, is short-lived, lasting only 2 to 5 minutes following bolus administration. Use of an etomidate infusion as a maintenance anesthetic provides excellent conditions for intraoperative monitoring of myogenic MEPS. Several authors have reported good success in obtaining potentials with continuous infusions of etomidate in the range of 10 to 30 µg/kg/min.⁵³,⁵⁴ Spinal potentials can be recorded following magnetoelectric stimulation of the motor cortex even after etomidate-induced EEG suppression.⁵⁵ The favorable effects of etomidate are thought to arise from its unique actions on the motor system at the spinal and supraspinal levels.⁵⁶ Etomidate disinhibits subcortical structures, including the extrapyramidal system, the brain stem, and the spinal cord, resulting in increased excitability of the motor system.⁵⁶,⁵⁷ Although depression of the adrenocortical axis is a known complication of etomidate infusion, the possibility of postoperative adrenocortical suppression must be weighed against the benefits of minimal MEP depression offered by etomidate.⁵⁸

Ketamine

Ketamine used as an infusion or a low-dose bolus has minimal effects on myogenic MEP responses. Both continuous infusions of ketamine (1-4 mg/kg/h) and intermittent boluses of ketamine (up to 0.5 mg/kg) used to supplement nitrous/narcotic anesthesia have been demonstrated to be compatible with intraoperative monitoring of motor potentials.⁴⁹,⁵⁴,⁵⁹,⁶⁰ Higher doses of 4 to 8 mg/kg have been shown to cause a moderate depression of CMAP amplitudes (4540% of baseline) in animal models.⁶¹

Unfortunately, ketamine has a high incidence of psychodelic side effects, such as emergence delirium, hallucinations, and unpleasant dreaming. Kawaguchi et al⁵⁹ reported psychodelic effects in 41% of patients receiving ketamine/narcotic infusions and inhaled N₂O. Again, the risk of the potential side
effects should be weighed against the risk of motor injury related to the planned procedure and the monitoring needs of the patient. Patients with preoperative motor weakness require less suppressive anesthetic agents like ketamine to obtain MEP potentials under anesthesia. The addition of low-dose propofol (15–50 μg/kg/min) to a ketamine infusion significantly reduced the incidence of psychotropic side effects to 14% of patients. However, propofol infusion doses higher than 30 μg/kg/min will also decrease monitoring success, even in the presence of a 5-pulse stimulus technique.

**Opioids**

Opioids are commonly used to supplement anesthetic agents during motor monitoring and have only minimal effects on myogenic potentials when used as a low-dose, continuous infusion. Although opioids are known to cause suppression of cortical excitation, they appear to have little effect on transmission at the dorsal horn. Fentanyl used alone in sedative doses (3 mcg/kg) produces no significant change in the latency or amplitude of human CMAPs evoked by transcranial electric or magnetic stimulation. Larger doses of fentanyl (8 mcg/kg) increased variability in the latency and amplitudes of single-pulse elicited CMAP in healthy volunteers. Despite this variability, potentials were reliably obtained in all patients.

In the presence of general anesthetics, bolus doses of fentanyl and morphine have been noted to cause prolonged CMAP amplitude depression. Animal data suggest that fentanyl, sufentanil, and alfentanil are about equal in their suppression of CMAP responses following bolus injection. As expected with its longer half-life, the depressive effects of fentanyl last significantly longer (15 minutes) than other agents.

Dose-dependent CMAP depression (50% of baseline) occurs with opioid infusions adequate to produce surgical anesthesia with narcotics alone; however, responses are not abolished until serum levels reach twice surgical anesthesia concentrations. Animal data suggest that remifentanil is less suppressive than other opioids. The serum level required to ablate myogenic responses is 20 times higher than that required for surgical anesthesia. Recent studies in humans have shown some dose-dependent reduction with remifentanil used as a single agent. At levels required for loss of responsiveness in 50% of patients (9 ng/mL [0.35 μg/kg/min]), CMAP amplitudes were reduced to 50% of baseline. However, potentials could still be followed with single-pulse stimulation even at plasma concentrations of 15 ng/mL (0.6 μg/kg/min).

**Benzodiazepines**

Benzodiazepines can cause CMAP amplitude depression but are less depressive than propofol or thiopental. Diazepam (0.17 mg/kg) has been found to have little effect on the MEP stimulus threshold, latency or amplitudes of myogenic tCM MEP when used as an anesthetic premedication. Bolus dosing of midazolam had previously been reported to decrease single-pulse elicited CMAP responses for up to 30 minutes following administration. However, more recent animal data demonstrated no significant effects of midazolam boluses when multi-pulse stimuli were used. Infusions of 0.1 mg/kg/h of midazolam produced no change in myogenic amplitudes or latency when used to supplement nondepressive anesthetics such as ketamine.

**Neuromuscular Blockade**

Although neuromuscular blockade was initially avoided during monitoring of myogenic MEPs, adequate monitoring conditions can be obtained during partial neuromuscular blockade. Accurate assessment of neuromuscular blockade is necessary to maintain the balance between surgical relaxation requirements and adequate CMAP responses. Comparing electromyographic responses induced by an electrical stimulus applied to the peripheral nerve (M-response) before and after relaxation gives an accurate reflection of the degree of blockade at the neuromuscular junction. Using single-twitch M-responses to maintain a single twitch height (T1) of 20% to 50% of baseline facilitates surgery while allowing for reproducible CMAP responses. Higher levels of neuromuscular blockade (5–10% of baseline) cause smaller amplitude potentials with greater trial-to-trial variability. Maintenance of a larger T1 height (44–55% of baseline) and a 6-pulse stimulus regimen has been shown to reduce response variation by 12% and to produce amplitudes similar in size to nonparalyzed conditions.

Partial neuromuscular blockade should be used with caution in patients with preoperative neurologic dysfunction. Lang et al. found that patients with preoperative motor deficits demonstrated greater amplitude reductions after partial neuromuscular blockade than patients with normal preoperative motor function (mean 419 μV vs. 1,670 μV).

The level of neuromuscular blockade should be monitored in the same muscle group from which CMAP responses are obtained. M-responses are more accurate in assessing the effects of neuromuscular blockade on CMAP response than twitch monitoring by accelerometer at the thenar eminence. During increasing neuromuscular blockade, M-response amplitudes in the target muscle group show a linear correlation with CMAP amplitudes, while the thenar twitch is more profoundly depressed.

M-responses can be used to differentiate between neurologic injury and increasing neuromuscular blockade. When monitoring combined transcranial CMAP and M-responses, reductions in both the CMAP and M-response potentials would suggest accumulating neuromuscular blockade due to muscle relaxants, whereas an unchanged M-response associated with a decreasing CMAP amplitude would indicate motor tract injury or inhibition at a site more proximal than the neuromuscular junction.
PHYSIOLOGIC INFLUENCES

Temperature

Temperature-dependent alterations in nerve conduction velocity result in latency changes in MEPs. Several animal models have demonstrated a linear increase in latencies of the myogenic, neurogenic, and evoked spinal cord MEP potentials during hypothermia. The stimulation threshold also increases with decreasing temperature, reflecting a cold-induced decrease in motor cortical excitability. Latency prolongation of spinal MEPs in rats suggests that spinal conduction velocity is decreased by 1.5 m/s per degree centigrade. Hypothermia induced in animal models demonstrates a biphasic effect on the amplitude of CMAP responses. Amplitudes initially increase in size, peaking at 29°C, and then progressively decrease until they are lost at 22°C. Despite these temperature effects on CMAP, time to detection of spinal cord ischemia was not different in hypothermic versus normothermic animals.

Anecdotal evidence in humans suggest that reproducible myogenic MEP waveforms can be obtained during mild hypothermia to temperatures of 31 to 34°C, although latencies increase below 32°C. Loss of spinal MEP potentials has been reported at 25°C in patients under circulatory arrest. Rewarming to normothermia reversed the effects of hypothermia and shortened MEP latencies.

Regional spinal hyperthermia above 42°C slightly increases MEP latency. MEP waveform amplitudes decrease with body temperatures greater than 38°C. When spinal cord temperatures exceed 45°C, amplitude reduction becomes irreversible, suggesting that permanent neural injury occurs at these temperatures.

Hypoxia

Little is known about the effects of hypoxia on human MEP responses. In animals, CMAP amplitudes remained unchanged until the inhaled oxygen concentration reached 10%. At this level of hypoxemia, 27% of animals lost MEP waveforms. The remaining animals showed a trend toward increased response latencies and depressed amplitudes, but the changes were not significant. MEP waveforms were lost in all animals only under extreme hypoxic conditions, with inhaled oxygen concentrations of 5.25%. This study suggested that CMAP responses are not significantly affected by hypoxia until the partial pressure of oxygen in the tissue reaches levels that have been associated with loss of ATP and cellular function. It is likely that critical reduction of neuronal tissue oxygenation by either decreased inspired concentrations of oxygen or by reduced oxygen delivery inhibits MEP potentials by disturbing oxidative metabolism and cell homeostasis.

Hypotension

Mild to moderate reductions in blood pressure do not induce MEP changes. Controlled hypotension in porcine models showed no significant decrease in spinal sciatic NMEP amplitudes until mean arterial pressures were decreased to below 50 mmHg.

The effect of hypotension on MEP in humans has been investigated with comparisons to normotensive controls. Reliable and reproducible spinal MEP potentials have been obtained in humans undergoing spinal surgery during Deliberate hypotension to mean arterial pressures of 60 to 70 mmHg.

Ischemia

Muscle responses generated by transcranial stimuli reflect cellular function at the level of the cortex, spinal cord, and muscle. Ischemia at any of these sites affects CMAP response amplitudes. In baboons, MEP changes induced by cortical ischemia were found to occur after reduction of cerebral blood flow to less than 16 mL/min/100 g. Ischemia of the lower limb muscles following aortic or femoral cross-clamping will cause loss of myogenic responses within 30 minutes of occlusion. Spinal cord ischemia induced by complete aortic occlusion will cause loss of myogenic responses within 2 minutes of occlusion. In contrast, spinal responses are reduced to only 40% of baseline after 25 minutes of spinal cord ischemia.

Hyper- and Hypocapnia

Hypercapnia has been found to have depressive effects on cortical and anterior horn cell excitability, as well as peripheral neuromuscular transmission. However, clinically significant changes in MEP waveforms do not occur until extreme levels of CO2 elevation are reached. In animals, changes in the latency or amplitude of the spinally elicited, sciatic MEP did not occur until PaCO2 reached 70 mmHg. During transcranial stimulation, response amplitude and latency changes were seen only when PaCO2 levels increased beyond 100 mmHg.

Hypocapnia may facilitate cellular transmission at the spinal level but has a slight inhibitory effect at the level of neuromuscular transmission. These opposing effects result in minimal effect on evoked responses. Both animal and human models have demonstrated no alterations in myogenic MEP after hyperventilation to an end-tidal CO2 between 13 and 30 mmHg.

IMPLICATIONS FOR PERIOPERATIVE MONITORING

Multistimulus techniques have greatly improved the success of intraoperative MEP monitoring under general anesthesia. Providing an adequate atmosphere for motor monitoring requires maintenance of a stable anesthetic concentration and physiologic milieu. The anesthetic protocol used should take into consideration the overall requirements of the patient and surgical procedure. Total intravenous anesthetic techniques comprising infusions of opioid and minimally depressive agents such as ketamine, etomidate, and midazolam will provide the greatest success for intraoperative MEP monitor-
ing. However, the undesirable side effects and pharmacokinetic properties of these agents can make them less than desirable in many patients. Use of higher pulse stimulus paradigms (3-6 pulses) can improve monitoring under more depressive agents with preferable pharmacologic profiles, such as propofol and isoflurane. However, these agents must be maintained at low doses for adequate monitoring conditions.

Bolus dosing of amnestic agents and opioids can cause long-lasting (15-20 minutes) depression or obliteration of MEP responses and should be avoided. A microcomputer-controlled closed-loop infusion system is useful to provide a stable anesthetic concentration and muscle relaxation.

Physiologic causes of response depression, such as severe anemia, hypotension, and hypoxia, should be quickly ruled out when MEP changes occur. Continuous monitoring rather than monitoring only during risky maneuvers will help detect gradual changes in baseline potentials caused by anesthetic or physiologic alterations. When possible, motor groups above and below the surgical field should be monitored to help to differentiate between systemic and local causes of waveform depression.

Spinal Surgery

A number of anesthetic regimens have been demonstrated to be acceptable during MEP monitoring in spinal surgical procedures. Intravenous infusions of ketamine, etomidate, methohexital, midazolam, and low-dose propofol, combined with opioids and partial neuromuscular blockade, have been effective in neurologically normal patients undergoing spinal surgery.

Patients with preoperative motor pathway injury may have very small baseline potentials, which can be obliterated by the addition of moderately depressive anesthetics. Consideration should be given to the use of less depressive agents in these patients, such as etomidate or ketamine added to an opioid infusion. Muscle relaxation has been suggested to cause greater MEP amplitude reduction in patients with pre-existing motor deficits and is probably best avoided. B1 bite blocks should be used in unrelaxed patients, as masseter muscle contraction will occur with transcranial stimulation and can lead to tongue laceration. Remifentanil has only recently been introduced as part of the regimen for intraoperative monitoring, but it may provide an excellent adjunct in situations where muscle relaxation must be avoided and minimal dosing of amnestic agents is required. The profound analgesic effect of remifentanil reduces anesthetic dose requirements. In addition, remifentanil has been shown to decrease movement in patients without neuromuscular blockade during highly stimulating procedures such as intubation. Maintaining a depth of anesthesia that minimizes patient movement is particularly important when movement could lead to serious injury, such as when the patient's head has been positioned in a rigid pin fixation device during cervical surgery.

Cranotomy

Anesthetic goals differ for spinal and intracranial surgery. Reduction of cerebral metabolism and blood flow is often required during craniotomy to provide adequate brain relaxation for surgical resection. Prompt emergence and minimal postoperative sedation are also required to monitor for neurologic sequelae. Ketamine has traditionally been avoided during intracranial surgery due to concerns about increased cerebral blood flow intraoperatively and postoperative psychodelic side effects, which can confound the neurologic examination. Low-dose propofol (25–50 μg/kg/min) and a short-acting narcotic can be used to satisfy the multiple requirements of craniotomy patients. However, the propofol dosing should be maintained at 50 μg/kg/min, and higher pulse stimuli regimens should be used for optimal monitoring. The short half-life and lack of accumulation make remifentanil an ideal opioid for avoiding excessive postoperative sedation after long procedures. Remifentanil is also useful for maintaining an adequate depth of anesthesia to avoid patient movement when the head position is fixed by rigid pins.

Direct stimulation of the cortex after craniotomy will overcome some volatile agent-induced MEP depression. Greater success in myogenic potential production has been demonstrated under combinations of volatile agents and N2O after direct cortical stimulation versus transcranial stimulation. The evidence suggests that physiologic manipulations often used as adjuncts to intraoperative management, such as controlled hypotension and mild hypothermia, generally do not decrease the reliability of motor monitoring.

Thoracic Aortic Reconstruction

MEP monitoring holds promise for reduction of postoperative paraplegia during thoracic aortic reconstruction (TAA). Myogenic MEP monitoring rapidly detects ventral horn ischemia and allows the surgeon to initiate strategies to improve spinal cord perfusion, such as intercostal artery reimplantation or increasing distal aortic perfusion pressures. Anesthetic requirements for surgical exposure, and the tendency for multiple comorbidity in this patient population, can make choosing an MEP-compatible anesthetic challenging during TAA repair. Agents that reduce myocardial contractility and cause hypotension are best avoided in patients undergoing TAA repair, as they often have widespread atherosclerotic disease. Various authors have reported success with the use of high-dose narcotic regimens supplemented by N2O, benzodiazepines, ketamine, or low-dose propofol for anesthesia.

Partial muscle relaxation may be necessary for adequate exposure during the transthoracic approach and to facilitate single-lung ventilation. Stinson et al found that maintaining neuromuscular relaxation at less than 80% inhibition (based on the amplitude of a single-twitch elicited EMG response) was inadequate for surgical exposure, and greater than 90% ablated...
MEP responses. Closed-loop infusions systems may be especially useful to maintain relaxation in this narrow range.

Retrograde arterial perfusion via a femoral catheter impedes bilateral motor monitoring by causing ischemia of the ipsilateral leg. Concomitant monitoring of SSEPs can help differentiate between limb and spinal cord ischemia. Loss of the peripheral nerve SSEP response will indicate limb ischemia as a cause of lost myogenic responses. Monitoring upper and lower extremity MEP and SSEP responses will also help distinguish systemic causes of response depression from spinal cord ischemia.

CONCLUSIONS

MEP monitoring for reduction of postoperative neurologic deficits requires an anesthetic tailored to optimize recorded responses. Preoperative planning and cooperation between the surgeon, anesthesiologist, and neurophysiologist are imperative to establish an optimal environment for monitoring motor potentials.

REFERENCES


