Anesthesia for Intraoperative Neurophysiologic Monitoring of the Spinal Cord

*Tod B. Sloan and †Eric J. Heyer

*University of Texas Health Science Center at San Antonio, Texas; and †Columbia University, New York, New York, U.S.A.

Summary: Intraoperative neurophysiologic monitoring (INM) using somatosensory and motor evoked potentials (MEPs) has become popular to reduce neural risk and to improve intraoperative surgical decision making. Intraoperative neurophysiologic monitoring is affected by the choice and management of the anesthetic agents chosen. Because inhalational and intravenous anesthetic agents have effects on neural synaptic and axonal functional activities, the anesthetic effect on any given response will depend on the pathway affected and the mechanism of action of the anesthetic agent (i.e., direct inhibition or indirect effects based on changes in the balance of inhibitory or excitatory inputs). In general, responses that are more highly dependent on synaptic function will have more marked reductions in amplitude and increases in latency as a result of the synaptic effects of inhalational anesthetic agents and similar effects at higher doses of intravenous agents. Hence, recording cortical somatosensory evoked potentials and myogenic MEPs requires critical anesthetic choices for INM. The management of the physiologic milieu is also important as central nervous system blood flow, intracranial pressure, blood rheology, temperature, and arterial carbon dioxide partial pressure produce alterations in the responses consistent with the support of neural functioning. Finally, the management of pharmacologic neuromuscular blockade is critical to myogenic MEP recording in which some blockade may be desirable for surgery but excessive blockade may eliminate responses. A close working relationship of the monitoring team, the anesthesiologist, and the surgeon is key to the successful conduct and interpretation of INM. Key Words: Anesthesia—Motor evoked potentials—Somatosensory evoked potentials—Muscle relaxation.
integrity more completely, both SSEPs and MEPs are monitored together. However, monitoring the spinal cord with MEPs is particularly challenging because anesthetic agents easily abolish the potentials elicited.

The purpose of this review is to describe the anesthetic issues that must be considered when using MEPs to monitor the central nervous system. We describe the anesthetic effects, physiologic effects, and then the anesthetic considerations required to optimize MEP monitoring. Because SSEPs are almost always monitored in conjunction with MEPs (Legatt, 2002), the effects of anesthetics on these potentials are also discussed.

OVERVIEW OF ANESTHETIC EFFECTS ON SENSORY AND MOTOR PATHWAYS

Mechanism of Action of Anesthetic Agents

The impact of anesthetic agents on neurophysiologic monitoring increases with the number of synapses in the pathway monitored because all anesthetic agents produce effects by altering neuronal excitability through changes in synaptic function or axonal conduction (Sloan, 2002a). An increased number of synapses in the pathway may account for why cortically generated evoked potentials are more sensitive to anesthetics than subcortical signals such as P14, N18/ P31, N34 signals. These differences may be important especially when there is a loss of cortical signals without changes in their subcortical counterparts. By examining the specific anesthetic agents, we can gain some insight into their mechanisms of effect and therefore methods for the choice of agents when monitoring is performed.

All anesthetics are either gaseous (inhaled) or dissolvable in fluids (intravenous). The gaseous agents are either “potent” inhalational agents like halothane, enflurane, isoflurane, sevoflurane, and desflurane, which are effective at relatively low concentrations (<10%), or the less “potent” inhalational agent nitrous oxide, which is used at higher concentrations (usually more than 50%). These potent inhalational agents produce their actions either by altering specific receptors (Flood and Role, 1998) or through nonspecific effects on cell membranes that alter the conformation structure of the receptor or ion channel at the protein–lipid interface (Sloan, 2002a). For years it has been well-known that the potency of volatile anesthetics varies with lipophilicity, suggesting that the mechanism of anesthesia depends on changes in the membranes of tissue such as alterations in synaptic function.

The intravenous sedative agents used in anesthesia interact at a number of different receptors. For example, barbiturates, etomidate, althesin, propofol, and benzodiazepines act at specific receptors, primarily by enhancing the inhibitory effects of gamma-aminobutyric acid. These agents are known to bind specifically to the gamma-aminobutyric acid-a receptor, where activation increases chloride conductance, hyperpolarizing the membrane and producing synaptic inhibition (Sloan, 2002a).

Some intravenous agents also work by blocking the excitatory effects of glutamic acid (Macdonald and Barker, 1979; Sloan, 2002a). There are now at least four known types of receptors in this system named by the binding of specific substances: N-methyl-D-aspartate, α-amino-3-hydroxy-5-methyl-isoxazole propionic acid, quisqualate, and kainate. Ketamine appears to have its major action by inhibiting the N-methyl-D-aspartate receptor, thereby reducing sodium flux and intracellular calcium levels (O’Shaughnessy and Lodge, 1988). Similarly, most anesthetic agents interact at multiple receptors in numerous pathways such that the effect on evoked responses likely varies with the spectrum of specific receptors and pathways affected. For example, barbiturates upregulate the N-methyl-D-aspartate receptor and interact competitively with some of the other binding sites (Sloan, 2002a).

Some anesthetics also activate opioid receptors (mu, kappa, and delta). Opioids depress electroexcitability by increasing inward K+ current and depressing outward Na+ current via a G-protein mechanism linking the receptors to the ion channels (Nestler and Aghajanian, 1997). This mechanism is distinct from that of volatile and intravenous anesthetics and may explain the fact that opioids are unlike any other agent.

Finally, anesthetic agents act at the “n-type” acetylcholine receptors found at the neuromuscular junction. This is the primary site of action of the neuromuscular blocking agents. The potent inhalational anesthetics also interact with this receptor at the neuromuscular junction; however, their effect appears to be minimal for altering electrophysiologic recordings.

The effects of anesthetic agents are thus the result of direct inhibition of synaptic pathways or the result of indirect action on pathways by changing the balance of inhibitory or excitatory influences. Thus, the specific electrophysiologic responses that rely extensively on synaptic function will be most susceptible to anesthetics. Although most anesthetics depress evoked response amplitude and increase latency, some anesthetic agents (etomidate and ketamine) enhance both SSEP and MEP amplitudes, perhaps by attenuating inhibition (Sloan, 1997).
Therefore, anesthetic agents will affect pathways containing synapses and this effect will be more prominent as the number of synapses increases. For this reason, SSEP responses generated in cortical structures will be the more affected (i.e., more sensitive to many anesthetics than those generated at more peripheral sites such as the spinal cord or brainstem, where fewer synapses are involved) (Sloan, 1997) (Figs. 1 through 3). Also for the same reason, effects of anesthetic agents on EEG parallel the effects of anesthesia on cortical evoked potentials because both depend on cortical synapse activity (Sloan, 1999). Because most anesthetic drugs produce a dose-dependent depression of the EEG, they produce decreased amplitude and increased latency of cortical SSEPs (Sloan, 1997).

The motor pathways and MEPs are susceptible to anesthetic agents at three sites. The first is in the motor cortex. Stimulation of neurons associated with movement, such as the pyramidal cells, is either by direct stimulation of these cells, which leads to the production of “D waves,” or indirect stimulation via internuncial neurons, which leads to production of “I waves” (Day et al., 1987b, 1989). Both of these responses are seen in epidural recordings from the epidural space in the spine (Fig. 4). Direct stimulation can be accomplished by transcranial electrical or intense magnetic stimulation. The D waves produced are relatively unaffected by anesthetics because no synapses are involved in their production or propagation down the spinal cord. I waves can be generated by either transcranial electrical or transcranial magnetic stimulation. They require synaptic activity for their production because they arise from stimulation of internuncial neurons. Therefore, they are affected markedly by anesthetics.

The second site is in the anterior horn cell. At this location the D and I waves summate. If they are able to bring the cell to threshold, the anterior horn cell depo-
larizes, producing a peripheral nerve action potential. Stimulation of multiple neurons produce a compound muscle action potential (CMAP; Fig. 5). Partial synaptic blockade at the anterior horn cell, induced by anesthetics, may make it more difficult to reach threshold (Sloan, 2002b). The combined effect of anesthetics in blocking the generation of I waves in the cortex, and synaptic transmission at the spinal cord anterior horn cell reduce further the probability of generating a CMAP. At higher anesthetic doses, an even more profound synaptic block at the anterior horn cell may inhibit synaptic transmission regardless of the composition of the descending spinal cord volley of activity. These effects are greatest when transcranial magnetic stimulation is used to generate motor responses and are less with transcranial electrical stimulation because of the relative dependence of the former on internuncial synaptic depolarization.

The third site is at the neuromuscular junction. Fortunately, with the exception of neuromuscular blocking agents, anesthetic drugs have little effect at the neuromuscular junction.

**Action of Specific Anesthetic Agents**

**Gaseous Agents: Halogenated Inhalational Agents**

Perhaps the most common anesthetics in use today are the halogenated inhalational agents (desflurane, enfurane, halothane, isoflurane, and sevoflurane). All halogenated inhalational agents produce a dose-related increase in latency and reduction in the amplitude of the cortically recorded SSEPs. This effect varies from isoflurane (most potent), to enfurane (intermediate), to halothane (least potent) (Sloan, 1997). Studies with sevoflurane and desflurane suggest they are similar to isoflurane at a steady state, but because of their more rapid onset and offset of effect (both are more insoluble than isoflurane), they may appear to be more potent during periods when concentrations are increasing.

Halogenated inhalational agents may reduce SSEP amplitude and prolong latency recorded from the cortex to a greater degree than when these responses are recorded from electrodes located at the cervicomедullary junction, spinal cord, and peripheral nerve.

Motor evoked potentials recorded in muscle (myogenic) are abolished easily by halogenated inhalational agents (see Fig. 5). Single-pulse stimulation myogenic transcranial MEPs appear to be so easily abolished by inhalational agents that they are often unrecordable in the presence of these agents. When recordable, MEPs may occur only at low concentrations (e.g., >0.2 to 0.5% isoflurane). This effect of inhalational agents is likely the result of depression of synaptic transmission either in the anterior horn cell synapses on motor neurons or in the cortex on the internuncial synapses with a loss of I waves. Two observations support the effect of anesthetics on motor neurons. Halogenated inhalational agents...
reduce the H-reflex (Mavroudakis et al., 1994). The D waves recorded in the epidural space, before synapsing in either the anterior horn or the neuromuscular junction, are highly resistant to the effects of inhalational agents and are easily recordable at high, volatile anesthetic concentrations (Gugino et al., 1997) (see Fig. 4).

Because the D wave is resistant to anesthetic depression, the anesthetic effect at the anterior horn cell can be overcome at low anesthetic concentrations by high-frequency (multiple-pulse) transcranial stimulation (trains of stimuli with interstimulus intervals of 2 to 5 msec) (Kawaguchi et al., 1996; Pechstein et al., 1998). Under these circumstances the multiple D waves (and I waves if produced) summate at the anterior horn cell to generate a peripheral nerve action potential and subsequent myogenic response (Figs. 6 and 7). However, the best anesthetic plan is to avoid inhalational agents for optimal MEP monitoring even when using high-frequency stimulation technique (Pechstein et al., 1998).

Studies with direct spinal or epidural stimulation show minimal effects of anesthesia on neurogenic or myogenic responses (Nagle et al., 1996). However, this stimulation activates both sensory and motor pathways. Therefore, the concern is that the antidromically activated action potentials in the sensory fibers would reflexly stimulate motor neurons at lower spinal levels, bypassing the descending motor tracts, but producing a myogenic response nevertheless. Mochida et al. (1995) studied the responses in the peripheral nerve and muscle after epidural stimulation in the cat and found that the type of spinal cord stimulation and the anesthetic used may alter the balance of sensory and motor contributions to the peripheral nerve and muscle response from direct spinal stimulation. Recent studies suggest that with isoflurane anesthesia, the motor component is blocked preferentially, perhaps by interaction at the synapses in the anterior horn cell or by differential effects on conduction in the spinal tracts in humans (Deletis, 1993). These studies do not, however, clearly allow a recommendation of anesthesia that will promote preferentially the monitoring of motor pathways with direct spinal, epidural, or perispinal stimulation. For this reason, intraoperative neurophysiologic monitoring methods that rely on stimulation of the spinal cord may not monitor the motor pathways reliably.

**Nitrous Oxide**

Nitrous oxide reduces SSEP cortical amplitude and increases latency when used alone or when combined with halogenated inhalational agents or opioid agents. When compared at equipotent anesthetic concentrations, nitrous oxide produces more profound changes in cortical SSEPs and muscle recordings from transcranial mo-

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**FIG. 6.** Motor evoked potential responses recorded by an epidural electrode in a ketamine- and isoflurane-anesthetized baboon after transcranial electrical stimulation. Note that the effect of adding a second stimulation pulse to the cortex increases the number of waves in the epidural recording. Recordings taken using a Biologic Navigator (Biologic Inc., Mundelein, IL, USA) from a midthoracic bipolar epidural recording electrode placed percutaneously using an amplification of 2,000 and a bandpass filtration of 3 to 1,500 Hz. A single- or multiple-pulse (interstimulus interval, 2 msec) supramaximal stimulus was used at Cz to Fz using a Digitimer D185.

**FIG. 7.** Motor evoked potential responses recorded from the hypothenar muscles from a baboon with 1% isoflurane anesthesia when no MEP response is present when only one cortical stimulation pulse is used. A small response is present with two pulses and a substantial response occurs with three or more pulses. Recordings taken using a Biologic Navigator (Biologic Inc., Mundelein, IL, USA) from a midthoracic bipolar epidural recording electrode placed percutaneously using an amplification of 2,000 and a bandpass filtration of 3 to 1,500 Hz. A single- or multiple-pulse (interstimulus interval, 2 msec) supramaximal stimulus was used at Cz to Fz using a Digitimer D180A.
tor stimulation than any other inhalational anesthetic agent (Sloan, 1997). Like halogenated agents, effects on subcortical and peripheral sensory responses and on epidurally recorded MEPs are minimal.

Despite the depressant effect of nitrous oxide, it has been used with all types of evoked potential recordings, particularly when combined with opioids (“nitrous–narcotic” anesthetic technique). Nitrous oxide may be “context sensitive” in that the actual effects may vary depending on the other anesthetics already present. As with sevoflurane and desflurane, nitrous oxide is relatively insoluble, such that anesthetic effects can change rapidly when concentrations are varied intraoperatively.

**Intravenous Anesthetic Agents**

Most anesthesia techniques use a mixture of different anesthetic agents. For example, inhalational agents are often supplemented with opioids or intravenous sedatives (e.g., benzodiazepines, etomidate, droperidol, or propofol). If the inhalational agents need to be avoided completely, then analgesic and sedative intravenous agents can be combined to produce a total intravenous anesthetic (TIVA).

**Intravenous Analgesic Agents: Opioids**

The effects of the opioid analgesics (alfentanil, fentanyl, remifentanil, and sufentanil) on SSEPs and MEPs are less than with inhalational agents, making opioids important components of anesthetic planning for evoked potential monitoring. They produce minimal changes in spinal or subcortical SSEP recordings. There is some depression of amplitude and an increase of latency in the cortical responses, especially for the late cortical peaks (latencies more than 100 msec). As with systemic opioids, the spinal application of morphine or fentanyl for postoperative pain management produces minimal effects on the SSEP and fails to alter the H-reflex (Sloan, 1997). Studies with myogenic responses from MEPs with electrical and magnetic stimulation show only mild amplitude decreases and latency increases with the opioids. In fact, fentanyl may reduce background spontaneous muscle contractions and associated motor unit potentials, further improving myogenic responses.

**Special Intravenous Analgesic Agents: Ketamine**

The effects of ketamine on evoked responses also differ from those of inhalational agents. Ketamine can enhance cortical SSEP amplitude and MEP amplitude in muscle and spinal recorded responses after spinal stimulation (Kano and Shimoji, 1974; Schubert et al., 1990). This latter effect on muscle responses may be mediated by the same mechanisms that potentiate the H-reflex. However, effects on subcortical and peripheral SSEP responses are minimal, as are the effects on myogenic MEPs (Glassman et al., 1993). Because of these effects, ketamine is a desirable agent for monitoring responses that are usually difficult to record under anesthesia (e.g., myogenic MEPs). However, increases in intracranial pressure with intracranial pathology and hallucinations may limit the use of ketamine in certain patients.

**Sedative–Hypnotic Drugs**

Intravenous sedative agents are used frequently to induce or supplement opioid- and ketamine-based analgesia for TIVA to ensure adequate sedation, anxiolysis, and amnesia. Although ketamine produces some dissociative effects in addition to analgesia, supplementation of ketamine with sedative medications can reduce the risk of hallucinations.

**Droperidol**

When combined with fentanyl (“neurolept anesthesia”), droperidol appears to have minimal effects on myogenic MEPs (Sloan, 1997). Recent concerns about prolonged QT changes in the electrocardiogram and arrhythmias may reduce the use of this drug.

**Barbiturates**

Thiopental remains a popular drug for induction of anesthesia, although transient decreases in amplitude and increases in latency of cortical response occur immediately after induction. Longer latency cortical waves are most affected, whereas minimal effects are seen on the subcortical and peripheral responses. Studies with another barbiturate, phenobarbital, demonstrate that the SSEP is virtually unaffected at doses that produce coma (Drummond et al., 1985), and changes are not seen until doses are sufficient to produce cardiovascular collapse (Sloan, 1997). Barbiturates are not used commonly during recording of MEPs because the CMAP responses are unusually sensitive to barbiturates. Furthermore, the effect appears to be quite prolonged. In one study, the induction bolus eliminated the CMAP from the MEP for a period of 45 to 60 minutes (Glassman et al., 1993).
Benzodiazepines

Midazolam has desirable properties of amnesia and has been used for monitoring cortical SSEPs. Midazolam, in doses consistent with induction of anesthesia (0.2 mg/kg) and in the absence of other agents, produces a mild depression of cortical SSEP (Sloan et al., 1990) and minimal effects on subcortical and peripheral components. As with thiopental, midazolam produces prolonged, marked depression of MEPs, suggesting that it also may be a poor induction agent for MEP recording.

Etomidate

Like ketamine, etomidate increases the amplitude of cortical SSEP components after injection without changes in subcortical and peripheral sensory responses (Sloan, 1997). This amplitude increase appears coincident with myoclonus seen after administration of the drug, suggesting a heightened cortical excitability. A sustained amplitude increase with constant drug infusion has been used to enhance SSEP cortical recordings that otherwise could not be monitored (Sloan, 1988) and to enhance amplitude in MEPs (Kochs et al., 1986). Studies with MEPs have suggested that etomidate is an excellent agent for induction and monitoring of CMAP responses. Of several intravenous agents studied, etomidate had the least degree of amplitude depression after induction doses or continual intravenous infusion. Thus, etomidate has been used for induction of anesthesia and as a component of TIVA, combined with opioids.

Propofol

Propofol induction produces amplitude depression in cortical SSEPs with rapid recovery after termination of infusion (Kalkman et al., 1992b). When the SSEP is recorded in the epidural space, propofol has no notable effect (Angel and LeBeau, 1992). Studies with electrical or magnetic elicited MEPs have demonstrated a depressant effect on response amplitude, consistent with a cortical effect (Kalkman et al., 1992a) (Fig. 8). Although propofol does not appear to enhance cortical responses, rapid metabolism allows rapid adjustment of the depth of anesthesia and effects on evoked responses. As a component of TIVA, infusions of propofol have been combined with opioids and have produced acceptable conditions for monitoring of cortical SSEPs and myogenic MEPs (Calancie et al., 1998; Pechstein et al., 1998). Because of this ability to titrate the dose rapidly, it has become an extremely popular agent in TIVA.

Muscle Relaxants

Because muscle relaxants have their major site of action at the neuromuscular junction, they have little effect on electrophysiologic recordings such as SSEPs, which do not derive from muscle activity. However, profound neuromuscular blockade will prevent recording of the CMAP during myogenic MEP monitoring. Furthermore, partial neuromuscular blockade has the benefit of reducing a substantial portion of patient movement, which accompanies the testing, and facilitates surgical procedures when muscle relaxation is needed for retraction of tissues.

Two methods are used customarily to assess the degree of neuromuscular blockade. The method that best quantitates the blockade involves measuring the amplitude of the CMAP produced by supramaximal stimulation of a peripheral motor nerve (M wave) called T1 and compares the amplitude with the baseline amplitude before adding the blocking agent. When neuromuscular monitoring is conducted this way, successful monitoring of myogenic responses has been accomplished at T1 between 5% and 50% of baseline (Sloan, 2002b).

A second technique is referred to as the train-of-four (TOF) response because it involves examining the muscle response when four peripheral motor nerve stimuli are delivered at a rate of 2 Hz. In this technique the amount of acetylcholine released decreases with each
stimulation such that its effectiveness to compete with the neuromuscular blocking agent is reduced with each stimulation. Quantitatively the TOF can be measured by comparing the amplitude of the M wave of the fourth twitch (T₄) with that of the first (T₁) in the T₄:T₁ ratio. Practically, the number of visible twitches produced is usually recorded with declining numbers of twitches as the blockade increases. Acceptable CMAP monitoring has been conducted with two of four twitches remaining. For comparison of the two techniques, only one response of four is present when T₁ is less than 10%, two twitches at 10 to 20%, and three twitches at 20 to 25% of the baseline T₁ response.

When using a neuromuscular blockade, tight control of the blockade is necessary so that excessive blockade does not eliminate the ability to record MEPs, thereby mimicking neural injury. For this reason, most clinicians use drug infusions, some with closed-loop control systems, to monitor the twitch and to control the infusion. In particular, the avoidance of drug boluses is important to prevent wide changes in relaxation, especially excessive degrees of block.

Although recording of myogenic MEP responses is possible with partial neuromuscular blockade, the amplitude of the CMAP will be reduced by the blockade. Studies suggest the actual reduction is nonlinear, with the M wave being reduced more than the MEP (Sloan, 2002b). Several studies have demonstrated that the MEP amplitude at a T₁ reduced to 20% of baseline correlates with an MEP reduction of 50 to 60% (Kalkman et al., 1992a; Sloan and Erian, 1993a, b) (Fig. 9).

Furthermore, when mechanical measurements are used (TOF), MEPs have been observed when no mechanical response was observed (Kalkman et al., 1992a). This nonlinearity can be explained by the observation that the mechanisms of muscle activation differ between the M response from supramaximal peripheral nerve stimulation (as used for measuring neuromuscular blockade) and the MEP response from transcranial stimulation. The MEP response is much larger because centrally applied pulses lead to repetitive activation of spinal motor neurons, with attendant spatial and temporal summation (Day et al., 1987a). For this reason, MEPs are more robust than the M response during blockade and may not be abolished as markedly as the M response (T₁).

In general, the goal with transcranial MEP testing is to have sufficient blockade such that patient movement with stimulation is not distracting or hazardous during the surgery (particularly when the microscope is used). Furthermore, some muscle relaxation may be necessary to allow surgical manipulation of structures adherent to muscles. In other circumstances, muscle relaxation may be necessary to reduce the noise in recording electrodes (e.g., SSEPs recorded near neck or facial muscles [see Fig. 3] or neurogenic responses recorded epidurally [Fig.
ings of MEP). A T1 blockade of 10 to 20% of baseline appears to accomplish this goal adequately (as mentioned earlier, this corresponds to two of four twitches in a TOF).

For monitoring, the blockade needs to be such that the remaining MEP amplitude is distinguishable reliably from the background noise. Currently, most authors recommended a blockade with T1 between 10 and 20% of baseline or one to two twitches in a TOF. A more profound block reduces the MEP excessively and a less profound block is associated with excessive patient movement. Because of varying muscle sensitivity to muscle relaxants, the neuromuscular blockade should be evaluated in the specific muscle groups used for electrophysiologic monitoring.

As a consequence of the amplitude reduction, the ability to record with partial neuromuscular blockade will be dependent on other factors that reduce the myogenic response amplitude, such as anesthesia or neurologic disease. Hence, amplitude reduction with initially small responses, or with anesthetic choices that reduce amplitude markedly, may make the use of a blockade more difficult. Fortunately the CMAP amplitude is usually quite large. It is also important to recognize that the use of amplitude criteria for warning of impending neurologic injury may not be possible because inevitable fluctuations in the degree of blockade may obscure the application of strict criteria. For this reason, some intraoperative neurophysiologic monitoring of MEPs use only the presence or absence of a response rather than amplitude criteria or attempting to “calibrate” the MEP amplitude based on the size of the M wave response.

Insufficient data are available for determining the expected impact of neuromuscular blocking agents when intraoperative neurophysiologic monitoring is used for evaluating electromyographic responses from mechanical irritation or spontaneous activity (such as with facial nerve monitoring or during cauda equina or spinal nerve root procedures). In these cases concern has been raised that mechanical stimulation of the nerve root may be a weak stimulus or that partial paralysis may reduce the ability to record these responses. In addition, patient motion is less of an issue. Motion, if it occurred, could provide direct positive feedback to the surgeon as he works around the nerve or when he intentionally stimulates to check nerve integrity. In these cases patient movement is anticipated by the surgeon (as opposed to unexpected motion during spinal or other surgeries when the stimulation is under the control of the monitoring team). Similar circumstances apply to the surgical testing of pedicle screw or nerve root testing during spinal surgery, and many monitoring teams elect to avoid muscle relaxants. With respect to the spinal procedures, if a partial neuromuscular blockade is used, the surgeon may be able to stimulate nearby nerve roots (e.g., adjacent levels of the spine) to identify whether recording is possible to confirm the probability of the monitoring being useful.

Nonanesthetic Intraoperative Factors Affecting Monitoring

In addition to changes resulting from the surgical manipulation of the nervous system and anesthetic effects, the physiologic milieu plays an important role in neuronal functioning. In addition, the interaction of this physiology and the surgical manipulation may determine neuronal survival.

Blood Flow

Maintenance and control of the patient’s blood pressure is part of the anesthetic management of the patient having surgery. Numerous studies have demonstrated a threshold relationship between regional cerebral blood flow and cortical evoked responses (Sloan, 1997). The cortical SSEP remains normal until blood flow is reduced to approximately 20 mL/min/100 g. At more restricted blood flows of between 15 and 18 mL/min/100 g of tissue, the SSEP is altered and lost. As with anesthetic effects, subcortical responses appear less sensitive than cortical responses to reductions in blood flow.

Local factors may produce regional ischemia not predicted by systemic blood pressure. For example, during spinal surgery, the effects of hypotension may be aggravated by spinal distraction, such that an acceptable limit of systemic hypotension cannot be determined without monitoring (Brodkey et al., 1972; Dolan et al., 1980; Gregory et al., 1979). Other examples of regional effects include peripheral nerve ischemia from positioning, tourniquets, or vascular interruption; spinal cord ischemia from aortic interruption or mechanical distortion; carotid artery interruption; vertebrobasilar insufficiency aggravated by head extension; cerebral artery constriction by vasospasm; and cerebral ischemia resulting from retractor pressure.

Motor evoked potentials and SSEPs are both sensitive to spinal cord events produced by vascular ischemia (aortic cross-clamping) or mechanical compression (epidural balloon). However, because these tracts are removed topographically from one another, MEPs and

SSEPs may show differential sensitivity to an ischemic event. The SSEP and the myogenic MEP are sensitive to spinal cord ischemia associated with thoracic aortic clamping and reductions in spinal cord blood flow.

**Intracranial Pressure**

Elevated intracranial pressure is associated with reductions in amplitude and increases in latency of cortically generated SSEPs (Mackey–Hargardine and Hall, 1985). Increased intracranial pressure, probably by virtue of its affect on cortical structures, produces a pressure-related decrease in cortical SSEP responses, with loss of brainstem responses as uncal herniation occurs. For MEPs, a gradual increase in the onset of the response occurs until a response can no longer be produced.

**Blood Rheology**

Because changes in hematocrit can alter both oxygen carrying capacity and blood viscosity, the maximum oxygen delivery is often thought to occur in a midrange hematocrit (30 to 32%). Evoked response changes with hematocrit are consistent with this optimum range. In a study of upper extremity SSEPs in the baboon, Nagao et al. (1978) observed an increase in amplitude with mild anemia, an increase in latency at hematocrits of 10 to 15%, and further latency changes and amplitude reductions at hematocrits less than 10%. These changes were partially restored by an increase in the hematocrit. Similar MEP data are not available.

**Ventilation**

Hypoxemia can also cause evoked potential deterioration (Grundy et al., 1981) before other clinical parameters are changed. Alterations in carbon dioxide are known to alter spinal cord and cortical blood flow. The most notable changes in cortical SSEPs occur when the carbon dioxide tension is extremely low, suggesting excessive vasoconstriction may produce ischemia (carbon dioxide tensions < 20 mm Hg). This effect has been suggested to contribute to alterations in SSEPs during spinal surgery (Grundy et al., 1982) and may be expected to produce some MEP changes.

**Temperature**

Hypothermia-associated alterations in SSEPs and MEPs have been observed (Sloan, 1997). Like anesthetic effects and ischemia, changes are more prominent at the cephalic end of long neural tracts or in components of responses associated with multiple synaptic elements. Hence, SSEP responses recorded from peripheral nerves are affected minimally, whereas those produced by cortical structures are affected markedly. Motor evoked potential responses will have an increased onset with hypothermia from slowed conduction.

Changes in regional temperature can also occur, resulting in evoked response alterations that would not be predicted otherwise based on unchanged body (core) temperature. For example, cold irrigation solutions applied to the spinal cord, brainstem, or cortex cause evoked response changes routinely. Similarly, extremity cooling (as from cold intravenous solutions) can alter the SSEP originating from stimulation to a nerve from that limb.

With hypothermia, the MEP demonstrated a gradual increase in onset as esophageal temperature decreased from 38°C to 32°C. An increase in stimulation threshold was also observed at lower temperatures. This is consistent with both cortical initiation and peripheral conduction being affected by the drop in temperature (Sloan, 1991).

**Other Physiologic Variables**

Changes in a variety of other physiologic variables may produce alterations in the evoked responses during surgical monitoring. Marked reductions in total blood volume and increases in superior vena caval pressure during cardiopulmonary bypass have been associated with SSEP changes. Other changes in the neurochemical environment (e.g., changes in glucose, sodium, potas-

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**TABLE 1. Anesthetic sensitivity matrix**

<table>
<thead>
<tr>
<th>Anesthetic effect</th>
<th>Sensitive to anesthetic agents</th>
<th>Relatively insensitive to anesthetic agents</th>
</tr>
</thead>
<tbody>
<tr>
<td>Insensitive to muscle relaxants</td>
<td>Group I: cortical SSEP*; cortical AEP*</td>
<td>Group II: epidural, and perispinal SSEP and MEP; far-field subcortical SSEP; sensory cranial nerve (BAEP)*</td>
</tr>
<tr>
<td>Sensitive to muscle relaxants</td>
<td>Group III: Transcranial MEP</td>
<td>Group IV: pedicle screw stimulation, spinal reflex testing, motor cranial nerve (e.g., facial nerve), and Spinal MEP*</td>
</tr>
</tbody>
</table>

* Cortical, epidural, perispinal, and subcortical somatosensory evoked potential (SSEP) and motor evoked potential (MEP) refer to the location of the recording electrodes.

‡ Spinal MEP refers to the proximal site of stimulation within the spinal cord with recording in the muscle.

AEP, auditory evoked potentials; BAEP, brainstem auditory evoked potentials.
 ANESTHETIC CHOICE AND MANAGEMENT

The choice of anesthesia for a surgical procedure in which electrophysiologic monitoring is to be performed depends on many factors. Foremost in the mind of the anesthesiologist is the safety and comfort of the patient. Some anesthetic choices will be dependent on the medical problems of the patient and some choices will be dependent on the specific surgical needs. Depending on the electrophysiologic monitoring modalities, constraints may occur on the choice of anesthetic agents or their doses.

The most effective approach to choose a suitable anesthetic technique is based on preoperative discussion of the case. In general, the modalities can be divided into four groups based on whether the responses recorded are sensitive or insensitive to anesthetic agents (primarily inhalational agents) and whether they are helped or hindered by muscle relaxants (Table 1). As is often the case when multiple modalities are to be monitored, the most restrictive aspects of each will define the anesthetic group, which determines the initial anesthetic approach.

Group I responses (sensitive to anesthetic agents but insensitive to muscle relaxants) represent the largest group of the more commonly recorded cortical sensory evoked responses. For monitoring during these modalities, the inhalational agents, if used, are usually restricted to less than 0.5 MAC of these agents. Current studies suggest that desflurane and sevoflurane may be desirable because their insolvability allows them to attain steady state faster with a change in concentration.

Some controversy exists regarding the use of nitrous oxide. As an agent that depresses the evoked potential by reducing amplitude and prolonging latency, it is often acceptable when combined solely with intravenous agents. However, when combined with the potent inhalational agents, it appears to produce a deleterious synergistic effect that produces more depression than would be predicted individually. Because nitrous oxide is relatively insoluble, the anesthetic effects can change rapidly when concentrations are varied. Increases in amplitude may be seen when nitrous oxide is discontinued abruptly (possibly obscuring a drop in amplitude, signaling neurologic deterioration, which occurred during the procedure).

Fortunately, group I responses are less affected by intravenous anesthetic agents. For example, opioids show mild depression of amplitude and increase in latency in cortical responses such that opioid analgesia is used commonly during recording of cortical SSEPs as a component of a total intravenous technique or as a supplement to a reduced concentration of inhalational agent. Ketamine is an example of an agent that permits recording of evoked responses and, in fact, may increase the cortical response amplitude (Schubert et al., 1990).

Droperidol and midazolam can be used for sedation before induction of anesthesia. Droperidol appears to have minimal effects on response when combined with opioids. Midazolam (0.2 mg/kg) produces a mild depression of cortical SSEPs and minimal effects on subcortical and peripheral SSEPs. Because of midazolam's excellent amnestic qualities, an infusion can be used to maintain supplemental hypnosis during opioid or ketamine analgesia. Thiopental, propofol, and etomidate are used for induction of anesthesia. Thiopental can be used for induction with these responses, but newer agents have supplanted its use in TIVA. Although propofol induction produces amplitude depression in cortical SSEPs, with rapid recovery after termination of infusion (Sloan, 1997), it has become a popular component of TIVA because its rapid metabolism allows titration. Like ketamine, etomidate produces an amplitude increase of cortical components after injection (Kochs et al., 1986) with no changes in subcortical and peripheral sensory responses, making it a valuable component of TIVA as well. Although muscle relaxants have no direct effect on SSEPs, they may actually improve the quality of the recordings because electromyographic interference is reduced in electrodes near muscle groups (see Fig. 3).

Pathways that are less dependent on synaptic function, on which the effects of anesthetic agents are far less marked, generally characterize group II responses. Hence, most inhalational and intravenous anesthetics can be used. As a consequence of the difference between groups I and II, substantial interest has been in monitoring from recording electrodes placed in the spinal bony elements, in the subdural or epidural space, and from recording electrodes placed subcortically as an alternative to cortical SSEP recording for spine surgery. Problems with extracortical recordings have included marked variability resulting from motion and dislodgment by the surgeon as well as lost vigilance of events at locations other than the spine (e.g., cortical ischemia). The epidural technique has become commonplace in Japan and Europe, and despite its invasive nature, this technique appears remarkably safe and is preferred by some authors (Erwin and Erwin, 1993; Jones et al., 1983). Perispinal electrodes can also be used for recording after perispinal, epidural, and cortical stimulation (Stephen et al., 1966).

Hence, it is common practice to combine recordings.
from the subcortical locations to supplement cortical recordings during spine surgery. As such, if anesthetic or physiologic shifts alter the cortical response, the subcortical response may assist in determining whether the change is the result of adverse circumstances in the surgery site or the result of changes in the cortical regions. If the cortical responses are the only responses monitored, this differentiation may be difficult and inappropriate conclusions may be drawn.

Stimulation of the spinal cord and recording from the spinal cord or recording of the peripheral nerve from spinal stimulation appears to be a group II response. As discussed earlier, the anesthetic choice may affect the relative contributions of motor and sensory components.

Group III responses are clearly the most challenging for the anesthesiologist, because the need to limit muscle relaxation and avoid inhalational agents requires total intravenous anesthesia. As such, the major drawback of transcranial MEP has been the effects of anesthesia. Because the effects of opioids are minimal, opioid-based anesthesia is often used when myogenic transcranial MEPs are monitored. Fentanyl may reduce background spontaneous muscle contractions and associated motor unit potentials, which may improve muscle recordings. Ketamine may also produce an increase in the amplitude of muscle- and spinal-recorded responses after spinal stimulation (Kano and Shimoji, 1974), making it a desirable agent.

Thiopental and midazolam produce CMAP depression at doses less than those affecting the SSEP and lasting for a long period of time after bolus induction (e.g., 45 minutes), making them less desirable agents. Propofol has been used in MEP when the recordings are epidural; however, it needs careful titration to avoid depression of the myogenic MEP responses. Thus, when most anesthetic protocols can be used for epidural recordings, anesthesia techniques using etomidate, ketamine, propofol, and opioids are the most popular for muscle response recording.

Some controversy exists regarding the allowable degree of muscle relaxation. As discussed earlier, some individuals raise concern that any degree of relaxation may obscure electromyographic recordings elicited by mechanical irritation of the nerves or when pathology exists and may reduce amplitude in patients with small responses such that MEP may not be monitored. On the other hand, the patient motion that occurs with transcranial motor cortex stimulation can be excessive, and some degree of relaxation is therefore usually desirable. Furthermore, muscle relaxation may be of help to remove muscle artifacts in epidural recordings. This suggests that no generalizations can be made and each patient must be analyzed individually. Tightly controlled relaxation is needed to prevent shifts in amplitude (or loss of the response) when relaxation is used and monitoring of this relaxation in the muscles being monitored is desirable.

Current studies with high-frequency trains of transcranial stimuli (two to five pulses with an interstimulus interval of 2 to 5 msec) produces a more robust stimulation. Perhaps these techniques will permit the use of more anesthetics for transcranial-stimulated MEP. Although high-frequency stimulation would appear to allow the use of agents that reduce amplitude and prolong latency (notably low-dose inhalational agents), the authors of clinical studies using this technique currently recommend TIVA (Sloan, 2002b). Clearly this is an area of anesthesia and monitoring that awaits pharmacologic advances to allow a wider application of this monitoring technique.

Lastly, group IV responses are usually recorded easily because, although muscle relaxation is limited, the freedom to use inhalational agents makes anesthesia less challenging. Typical responses here are activation of cranial or peripheral nerves and recording of peripheral muscle responses (e.g., pedicle screw testing during spinal instrumentation). As discussed earlier, controversy surrounds the use of muscle relaxants. Some authors (Sloan, 2002b) have indicated that spontaneous activity from nerve irritation is difficult to detect during controlled relaxation. Small amplitude responses of injured or poorly functioning nerves are particularly difficult to detect, such that many authors recommend avoiding muscle relaxants in these cases. Stimulation of spinal cord proximal to areas of risk to produce myogenic MEPs is insensitive to the anesthetic technic (i.e., inhalational or TIVA) but sensitive to the degree of muscle relaxation.

Thus, based on the monitoring modalities involved, the basic anesthetic constraints can be identified. Usually the initial anesthetic choice becomes apparent, as mentioned earlier, and an initial maintenance anesthesia is delivered after induction. Before the period of critical monitoring, the monitoring team and the anesthesiologist need to assess the quality of the responses. If the anesthetic choice has allowed adequate responses, then the major goal of anesthesia is to maintain a steady state of anesthetic drugs so that fluctuations do not result in response variations that might obscure or simulate indications of neural compromise. If the electrophysiologic data are inadequate the monitoring team should evaluate whether the monitoring technique can be adjusted to allow adequate responses. For example, changes in recording electrodes, filter settings, and stimulation rate may improve the responses. Furthermore, shifting to a

technique that is less susceptible to anesthetics may permit success (e.g., monitoring using subcortical SSEPs instead of cortical SSEPs).

If the electrophysiologic technique cannot be adjusted, the anesthesiologist needs to determine whether a change in the anesthetic technique is possible to allow better recording. With group I modalities, the elimination of nitrous oxide and potent inhalational agents may permit evoked potential recording. If this is not successful, the anesthesiologist may wish to consider the use of etomate or ketamine to enhance the cortical responses. A similar situation applies to group III responses, in which the usual choice of TIVA may need to be adjusted to include etomate or ketamine. For responses affected by muscle relaxation (groups III and IV), careful evaluation of the relaxation is necessary.

In addition to maintaining a steady anesthetic state, the anesthesiologist should also seek to maintain a steady physiologic milieu. By integrating the electrophysiologic findings with physiologic and anesthetic monitoring, the anesthesia team can provide as optimal a neural environment as possible for the patient. Finally, by integrating our knowledge of the surgical procedure and these physiologic and anesthetic effects, the anesthesiologists can participate actively in the electrophysiologic monitoring team to interpret changes in the monitored responses and to assist surgeons in their operative decision making.

**CONCLUSION**

Although the choice and management of anesthesia is important to the success of intraoperative monitoring, the critical component of teamwork underlies the entire process. In fact, the entire operative team needs to remain focused on their interdependence in creating the most effective outcome for the patient. The interdependence of the surgeon and anesthesiologist is well known, and the interdependence of the surgeon with the monitoring team is logical. For example, the surgeon relies on the monitoring team to be his “electrophysiologic eyes and ears” whereas the monitoring team relies on the surgeon to keep them informed of the changing operative areas of risk so those eyes and ears can remain focused on the most appropriate area of neurologic risk.

However, often forgotten is the mutual interdependence of the monitoring team and the anesthesiologist. The monitoring team relies on the anesthesiologist to provide a physiologic and anesthetic milieu that is supportive of monitoring and to inform the monitoring team when untoward anesthetic and physiologic changes may result in changes in the monitoring that may obscure effective neurologic vigilance. In return, the anesthesiologist relies on the monitoring team to be her “neuropsychologic eyes and ears” to detect untoward physiologic compromise reflected in the monitoring and should suggest that the physiologic management be adjusted to improve the neural environment.

Clearly, a better understanding of the effects of anesthesia and physiology allows the monitoring team to work more effectively with the anesthesiologist. Likewise, a better understanding of electrophysiologic monitoring allows the anesthesiologist to integrate the results in decision making and physiologic management, improving patient care.

**REFERENCES**


