

# Intraoperative neurophysiological monitoring for the anaesthetist

## Part 2: A review of anaesthesia and its implications for intraoperative neurophysiological monitoring

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### Abstract

The use of intraoperative neurophysiological monitoring (INM) during spinal orthopaedic and neurosurgical procedures provides a challenge to the attending anaesthesiologist. Since all anaesthetic agents affect synaptic function, the choice of agent will be determined by the type of surgery and the INM modality employed. Halogenated volatile agents decrease evoked potential (EP) amplitude and increase latency, and should be avoided in modalities that pass through cortical tracts. The effect on EPs is apparent at minimum alveolar concentrations of 0.3-0.5. Intravenous agents affect EPs in a dose-dependent manner, and should be titrated to response. Total intravenous anaesthesia with propofol and remifentanyl is the preferred technique. The risk of propofol infusion syndrome has not been shown to affect the choice of this agent. Compound muscle action potentials are abolished by barbiturates, and should be avoided during motor-evoked potential (MEP) monitoring. Although somatosensory-evoked potentials are unaffected by muscle relaxants, they prevent the monitoring of MEPs and should be avoided during multimodal use. When paralysis is required to ensure patient safety, the train-of-four ratio should be kept at 2/4 twitches and a T1 response at 10-20% of baseline, with use of a closed-loop system.

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### Introduction

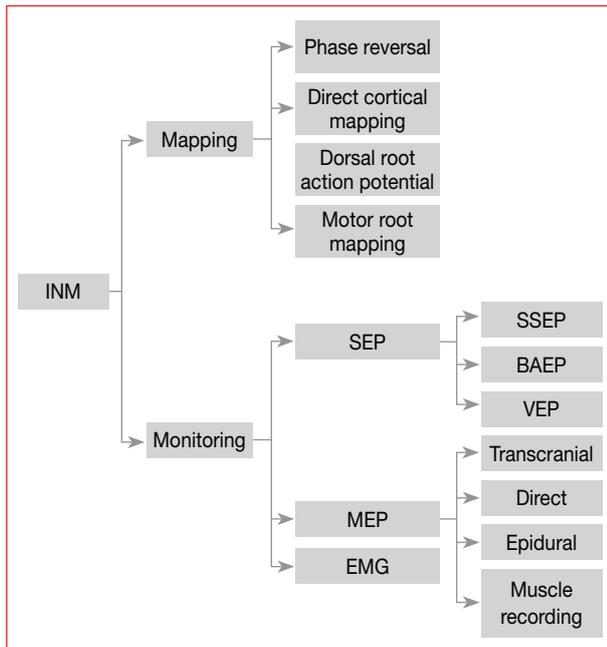
The use of intraoperative neurophysiological monitoring (INM) is fast becoming the gold standard in specialised neurosurgical and spinal centres throughout the world.<sup>1</sup> The progression from using somatosensory-evoked potentials (SSEPs) alone, to the multimodal use of both SSEPs and motor-evoked potentials (MEPs) to monitor both dorsal sensory pathways and the anterior corticospinal tracts, provides the optimum monitoring environment in which to prevent false negative and positive results.<sup>2</sup> The use of brainstem auditory-evoked potentials (BAEPs) for posterior fossa surgery, as well as cortical mapping techniques, provides a further buffer of safety when resecting tumours in highly sensitive areas. The use of anaesthetic agents has a direct impact on the quality of evoked potentials (EPs) elicited during INM. A poorly planned and executed anaesthetic could render EPs useless, and lead to poor outcome and surgical frustration. By focusing on key areas of the surgical endeavour to monitor nerve tracts, and by understanding how anaesthetic agents affect the various

signals, the anaesthesiologist will become a valuable role player in current and future developments in INM.<sup>3</sup> Because of the physiologically sensitive nervous system and different anaesthetic approaches employed in children, paediatric anaesthetic management of patients undergoing INM requires special consideration.<sup>4</sup> Anaesthetic agents also tend to be more potent and to have longer-lasting effects in children.<sup>2</sup>

Figure 1 provides a summary of intraoperative neurophysiological monitoring modalities.

### The effect of anaesthesia on evoked potentials

Since all anaesthetic agents target synaptic function, they all impact on INM.<sup>4</sup> Because of the different number of synapses in the monitored nerve tract, the different INM modalities do not share the same sensitivity to anaesthetic agents. The more synapses in the neurological pathway that is being monitored, the more marked the effect on latency and amplitude of the EPs.<sup>5</sup> Generally, anaesthetic agents



BAEPs: brainstem auditory-evoked potentials, EMG: electromyographic, INM: intraoperative neurophysiological monitoring, MEPs: motor-evoked potentials, SEP: sensory-evoked potentials, SSEPs: somatosensory-evoked potentials, VEPs: visually evoked potentials

**Figure 1:** Summary of intraoperative neurophysiological monitoring modalities

will cause an increase in latency and a decrease in the amplitude of EPs.<sup>5</sup>

Anaesthesia appears to have a fivefold impact on INM:<sup>4</sup>

- Altered synaptic function.
- Altered secondary pathways which suppress or enhance the primary pathway.
- A global effect on cortical and spinal cord neural processing.
- An effect of the neuromuscular agents (NMAs) at the neuromuscular junction (NMJ).
- Anaesthetic effect on the physiology that affects neural functioning, e.g. a change in blood pressure.

Visually evoked potentials (VEPs) appear to be the most affected by general anaesthesia, and because of their unreliable signal, are not a favoured technique for use during INM.<sup>6</sup> SSEPs are intermediate in sensitivity and depend on the type of agents used.<sup>5</sup> MEPs are dependent on a functioning NMJ, and may be totally abolished during the use of NMAs. Transcranial MEPs in children can be significantly depressed, with the use of halogenated agents at lower concentrations than those in adults.<sup>2</sup> BAEPs are the most resistant to anaesthesia. The early brainstem waves (< 10 ms latency) are more resistant to drugs than the early and late cortical responses (> 100 ms).<sup>6</sup>

## The effect of specific anaesthetic agents

### Inhalational anaesthetic agents

The halogenated volatile agents (sevoflurane, desflurane and isoflurane) are most often used today, and have been

shown to decrease EP amplitude and increase latency.<sup>5</sup> These dose-related changes are due to the synaptic effects on neural pathways, and affect SSEPs, notably when recorded from the cortex, MEPs recorded over muscle, and VEPs and BAEPs. The drastic effect on VEPs renders this modality useless in the presence of halogenated agents.<sup>4-6</sup>

Isoflurane has the most potent effect, and halothane the least. Some authors believe that sevoflurane and desflurane are as potent as isoflurane during a steady state. However, because they are less soluble, they may be more potent when concentrations are increasing.<sup>5</sup> This characteristic makes sevoflurane and desflurane useful during induction (sevoflurane) and maintenance (desflurane) because their concentration may be rapidly adjusted to minimise the effect of monitoring during surgery.<sup>4</sup> The effect on EPs can be apparent at 0.3-0.5 minimum alveolar concentrations (MAC). Because of the insoluble nature of sevoflurane and desflurane, the anaesthetic effect on INM can change rapidly when concentrations are changed.<sup>5</sup>

Because of its action on neuronal nicotinic acetylcholine receptors, nitrous oxide (N<sub>2</sub>O) may have a profound effect on EPs.<sup>4</sup>

Table I shows the effect of different anaesthetic agents on evoked potentials.

### Intravenous anaesthetic agents

All the intravenous anaesthetic agents cause a dose-dependent decreased amplitude and increased latency of the EP.<sup>6</sup> The effect is less marked than those seen with volatile agents. Therefore, to preserve neuronal function during INM, a combination of intravenous agents is often employed.<sup>4</sup> Because of the preservation of EPs, even with the use of high-dose opioids, total intravenous anaesthesia (TIVA) is favoured by many centres.<sup>5</sup>

#### Propofol

Propofol causes a decreased amplitude in cortical SSEPs and MEPs at high concentrations.<sup>4,5</sup> The drug can be rapidly titrated to levels that allow for recording of EPs because of rapid metabolism. Higher concentrations of propofol are often required to provide anaesthesia in children.<sup>4</sup> Some practitioners have added or replaced propofol with dexmedetomidine or ketamine to preserve EPs.<sup>4</sup> Propofol infusion syndrome has been described in children and adults during the use of prolonged, high-concentration propofol infusions.<sup>4</sup> It has become the anaesthetic agent of choice with TIVA. Its combined use with other sedative analgesic agents allows for the use of lower concentrations that preserve EPs and prevent propofol infusion syndrome.

#### Thiopentone

A transient decreased amplitude and increased latency of EPs is observed after induction with thiopentone.<sup>5</sup> The compound muscle action potentials (CMAPs) are very

**Table 1:** Effect of different anaesthetic agents on evoked potentials

Drug	Latency	Amplitude	Notes
Volatile agents	↑	↓	Isoflurane > sevoflurane or desflurane Effect at 0.3-0.5 MAC
Nitrous oxide	↑	↓	Potent effect on neuronal nicotinic acetylcholine receptors. Avoid
Propofol	↑ Dose-dependent	↑ Dose-dependent	Rapid metabolism allows titration during TIVA
Thiopentone	↑↑	↓↓	CMAP very sensitive to barbiturates
Etomidate	↓	↑	Use in combination with TIVA to enhance EP quality
Ketamine	↑	↑	Ketamine ↑ ICP Use in combination with TIVA to enhance EP quality
Midazolam	↑↑	↓↓	Prolonged marked suppression of MEPs
Dexmedetomidine	↑	↓	Used in combination with other agents to decrease dose of TIVA
Fentanyl	<ul style="list-style-type: none"> <li>• Preserved at high doses</li> <li>• Fentanyl at 60 µg/kg preserved SSEP</li> </ul>	<ul style="list-style-type: none"> <li>• Dose-dependent ↓</li> <li>• Fentanyl at 50 µg/kg</li> <li>• BAEPs preserved</li> </ul>	Preserved SSEPs and MEPs at high doses
Pethidine	Preserved EPs at high dose	SSEP amplitude	
Morphine	↑ Dose-dependent	↓	
Remifentanyl	Preserved	↓	Remifentanyl used in combination with isoflurane or TIVA. Rapid metabolism allows titration
Intrathecal opioids	SSEPs unaffected	Unaffected	
Muscle relaxants	MEPs abolished	MEPs abolished	Used to prevent patient movement during transcranial MEPs Used to ↓ EMG interference Keep T1 at 10-20% of baseline response Keep train of four at 2/4 twitches

BAEPs: brainstem auditory-evoked potentials, CMAP: compound muscle action potential, EMG: electromyographic, EPs: evoked potentials, ICP: intracranial pressure, MAC: minimum alveolar concentrations, MEPs: motor-evoked potentials, SSEPs: somatosensory-evoked potentials, TIVA: total intravenous anaesthesia, transcranial MEPs: transcranial motor-evoked potentials

sensitive to barbiturates and the effect is long lasting. Barbiturates should be avoided in cases in which MEPs are being recorded.

### Etomidate

Etomidate causes an increase in the amplitude of cortical SSEPs.<sup>5</sup> This effect coincides with the myoclonus observed during induction.<sup>5</sup> Etomidate has been used as an induction agent, with excellent results in cases involving MEPs and CMAPs. It has also been used as a component of TIVA at low doses, where amplitude enhancement can be observed.

### Ketamine

Increased cortical SSEP amplitude and MEP amplitude in muscle and the spinal cord has been observed with ketamine.<sup>5</sup> It is often used in combination with TIVA to enhance responses that are usually difficult to monitor under anaesthesia, e.g. myogenic MEPs. It is important to be aware of the raised intracranial pressure (ICP) that can occur in patients with cortical abnormalities, and the effect of raised ICP on cortical SSEPs.<sup>5</sup>

### Midazolam

A mild suppression of cortical SSEPs is seen at doses used for induction of anaesthesia (0.2 mg/kg).<sup>5</sup> Midazolam

should be avoided during monitoring of MEPs because of prolonged marked depression thereof.

### Dexmedetomidine

This selective central alpha 2-receptor agonist is increasingly being used for analgesia, anxiolysis, hypnosis and sedation.<sup>4</sup> When combined with other agents, it allows for the use of lower concentrations of anaesthetic agents during TIVA.<sup>5</sup> At low doses, the SSEPs and MEPs are preserved, but these are suppressed at higher doses.<sup>4</sup>

### Opioids

Opioids preserve SSEPs and MEPs at high doses. This allows for very good analgesia.<sup>4</sup> They cause a dose-dependent decrease in amplitude and increased latency.<sup>6</sup> Even at high doses (60 µg/kg), the use of fentanyl results in reproducible SSEPs, making it an ideal agent during INM. BAEPs remain resistant to fentanyl up to doses of 50 µg/kg.<sup>6</sup> Morphine causes a dose-dependent suppression of SSEPs, similar to fentanyl.<sup>6</sup> Pethidine has been shown to increase the amplitude of SSEPs.<sup>6</sup>

Remifentanyl, as part of TIVA, is often employed at an induction dose of 1 µg/kg, followed by an infusion combined with propofol or low-concentration isoflurane. It has a dose-dependent effect on EPs.<sup>6</sup> It is rapidly metabolised, allowing

for titration when EPs are suboptimal. Intrathecal fentanyl and morphine produce very little change to the SSEP.

### Muscle relaxants

Since SSEPs do not arise from muscle activity, they are unaffected by muscle relaxants.<sup>5</sup> NMAs act at the NMJ and prevent the recording of MEPs. To facilitate induction and intubation, some practitioners limit the use of NMAs to short-acting agents.<sup>4</sup> Patient movement during transcranial MEPs can be avoided by the use of titrated NMAs in drug infusions, often employed with a closed-loop control system.<sup>5</sup> The aim of NMA use during INM is to prevent patient movement, which can be hazardous while using a microscope, as well as to allow for surgical manipulation of the structures adherent to the muscle.<sup>5</sup> The use of NMAs may also improve some EPs by reducing electromyographic interference near the recording electrode.<sup>4</sup> When using NMAs in INM, monitoring of neuromuscular blockade is necessary. Two methods are employed. The best method is to measure the amplitude of the CMAP produced by a supramaximal stimulation of a peripheral motor nerve (T1) and to compare this with the baseline amplitude recorded prior to administration of the NMA. INM of the myogenic responses can successfully be recorded at T1 of 5-50% of baseline.<sup>5</sup> The train of four may also be used, with acceptable MEPs recorded with 2/4 twitches remaining.<sup>5</sup> Recording of MEPs remains possible with the use of NMAs, but the amplitude of the EPs is reduced in a nonlinear fashion.<sup>5</sup> It is recommended that the T1 response is kept at 10-20% of baseline, or two twitches in a train of four.<sup>5</sup>

Table II details physiological effects on evoked potentials.

**Table II:** Physiological effects on evoked potentials

Parameter	Effect
Blood flow	Cortical SSEPs ↓ at 20 ml/minute/100 g regional cerebral blood flow Cortical SSEPs lost at 15 ml/minute/100 g regional cerebral blood flow
Blood rheology	↑ Amplitude of SSEPs in mild anaemia: ↑ blood flow ↑ Latency of EPs at haematocrit of 10-15%
Blood glucose s-Sodium s-Potassium	Keep within normal values to ensure adequate neuronal function
Temperature	Cortical SSEPs are most sensitive MEPs ↑ latency at 32°C Cold irrigation of neuronal structures alters EPs
Intracranial pressure	↓ Amplitude and ↑ latency with raised intracranial pressure
Ventilation	Hypoxaemia alters EPs Altered SSEPs at pCO <sub>2</sub> < 20 mmHg

EPs: evoked potentials, MEPs: motor-evoked potentials, pCO<sub>2</sub>: partial pressure of carbon dioxide, SSEPs: somatosensory-evoked potentials

## Physiological and non-anaesthetic factors that affect evoked potentials

### Blood flow and blood pressure

Cortical SSEPs have been shown to decrease when regional cerebral blood flow falls below 20 ml/minute/100 g. The SSEP is lost below 15 ml/minute/100 g.<sup>5</sup> Additionally, SSEPs have been shown to be sensitive to blood pressure that is not usually associated with neural ischaemia. An acceptable blood pressure at the lower limit of normal autoregulation might already cause a drastic decline in SSEPs.<sup>4</sup> The local pressure effects of retractors, tourniquets and positioning might decrease the SSEPs at a higher blood pressure than anticipated.<sup>5</sup> A raised superior vena cava pressure and reduced blood volume will also alter the SSEP.

### Blood rheology

Oxygen delivery to tissue is dependent on blood viscosity, which is affected by the haematocrit. Maximum oxygen delivery occurs at a haematocrit of 30-32%. Because of increased blood flow, increased amplitudes of SSEP occur in mild anaemia, but there is an increased latency of EPs at haematocrits of 10-15%.<sup>5</sup>

Changes in the neurochemical milieu may also affect EPs. Therefore, blood glucose levels and electrolytes should be monitored and kept within normal parameters.<sup>5</sup>

### Temperature

Neural tracts with multiple synapses are most sensitive to hypothermia. SSEPs recorded from peripheral nerves appear less affected than recordings from cortical structures.<sup>5</sup> MEPs exhibit an increased latency, with oesophageal temperatures decreasing from 38°C to 32°C. Because of cold irrigation solutions applied to neural structures, unchanged core temperatures with regional changes in temperature can also lead to altered latency and amplitude.<sup>5</sup>

### Intracranial pressure

Because of the pressure-related effect on cortical structures, cortical SSEPs show reduced amplitudes and increased latency with elevations in intracranial pressure. MEPs suffer from increased intracranial pressure until eventually no EPs can be recorded.<sup>5</sup>

### Ventilation

The vasoconstrictive effects of hypocapnia may modify spinal and cortical blood flow, which can alter SSEPs at the partial pressure of carbon dioxide < 20 mmHg. Similarly hypoxaemia will also affect EPs.<sup>5</sup>

**Table III:** Effect of volatile agents and muscle relaxants on evoked potentials: planning the anaesthetic approach

Effect of anaesthesia on evoked potentials	Evoked potentials that are sensitive to volatile agents	Evoked potentials that are relatively insensitive to volatile agents
Evoked potentials that are insensitive to neuromuscular agents	<i>Group 1</i> <ul style="list-style-type: none"> <li>Cortical SSEP</li> <li>Cortical AEPs</li> </ul>	<i>Group 2</i> <ul style="list-style-type: none"> <li>Epidural and perispinal SSEPs and MEPs</li> <li>Far-field subcortical SSEPs</li> <li>BAEPs</li> </ul>
Anaesthetic approach	<i>Group 1</i> <ul style="list-style-type: none"> <li>Volatile &lt; 0.5 MAC</li> <li>Desflurane or sevoflurane</li> <li>Not affected by IV agents</li> <li>NMB may ↑ quality of EP</li> </ul>	<i>Group 2:</i> <ul style="list-style-type: none"> <li>Both volatile and IV agents safe to use</li> </ul>
Evoked potentials that are sensitive to neuromuscular agents	<i>Group 3</i> <ul style="list-style-type: none"> <li>Transcranial MEPs</li> </ul>	<i>Group 4</i> <ul style="list-style-type: none"> <li>Pedicle screw stimulation, spinal reflex testing, motor cranial nerve (e.g. facial nerve)</li> <li>Spinal MEPs</li> </ul>
Anaesthetic approach	<i>Group 3</i> <ul style="list-style-type: none"> <li>Limit use of volatile agents and NMBs</li> <li>If NMB used:</li> <li>Keep T1 at 10-20% of baseline and train of four 2/4</li> <li>TIVA requires careful titration of propofol. Monitor acid base and electrolytes</li> <li>Avoid barbiturates</li> </ul>	<i>Group 4</i> <ul style="list-style-type: none"> <li>Volatile agents may be used</li> <li>Avoid NMBs</li> </ul>

AEPs: auditory-evoked potentials, BAEPs: brainstem auditory-evoked potentials, EPs: evoked potentials, IV: intravenous, MAC: minimum alveolar concentrations, MEPs: motor-evoked potentials, NMBs: neuromuscular blockers, SSEPs: somatosensory-evoked potentials, TIVA: total intravenous anaesthesia

## Anaesthetic management during paediatric surgery

The anaesthetic approach is dictated by the type of surgery performed, the INM modality to be monitored, and by ensuring that patient safety and comfort is not compromised. In order to maintain a normal physiological environment that will not affect the quality of EPs,<sup>4,5</sup> the underlying medical condition of the patient will also determine anaesthetic choices. The most pertinent question is whether or not the use of NMAs and volatile agents will affect the outcome of INM. Preoperative discussion with the surgical team and neurophysiologist is of paramount importance in aiding the decision-making process.<sup>5</sup> The multimodal approach to INM, where both cortical SSEPs and transcranial MEPs are employed, will often make the use of NMAs and high concentration halogenated agents obsolete.

INM modalities can be divided into four groups (Table III). These are based on whether recorded responses are sensitive to anaesthetic agents: primarily volatile agents, and whether or not the use of NMA will abolish EPs.

Group 1 responses require the limitation of inhalational agents to < 0.5 MAC. Desflurane and sevoflurane achieve a steady state faster, and are therefore the agents of choice.<sup>5</sup> The use of N<sub>2</sub>O remains controversial, and should be avoided when used in combination with potent inhalational agents. Group 1 responses are minimally affected by intravenous agents and the use of a NMA may improve the quality of EPs by reducing electromyographic interference in electrodes near muscle groups.<sup>5</sup>

Group 2 responses are less dependent on synaptic function so inhalational and intravenous agents may be deployed. Because of the fact that these responses are less sensitive to anaesthetic agents, the use of epidural electrodes and subcortical electrodes is fast replacing cortical SSEPs during spinal surgery.<sup>5</sup>

Group 3 responses require limited use of NMAs and inhalational agents. Therefore, TIVA is the modality most often employed. The effect of opioids on MEPs is minimal, making opioid-based anaesthesia ideal.<sup>5</sup> Thiopentone and midazolam should be avoided in group 3 responses because of prolonged suppression of the CMAP.<sup>5</sup> Propofol concentrations require careful titration in TIVA to prevent marked suppression of the MEPs. The use of any form of NMAs remains a contentious issue. Many surgeons prefer NMAs to be omitted from the anaesthesia plan. When their use is absolutely indicated, tight titration of the T1 response between 10-20% of baseline or 2-3 twitches in a train of four is recommended.

Group 4 responses are less challenging and allow for the use of inhalational agents. Because of the sensitivity of injured or poorly functioning nerves, some practitioners avoid any use of NMA in this group.<sup>5</sup>

After induction and positioning of a patient, the neurophysiologist will take a baseline set of recordings. Therefore, the concentration of intravenous and inhalational agents should already be at steady state when these sets of data are obtained. After baseline data has been acquired, physiological and anaesthetic changes should be avoided.

Fluctuation of anaesthetic depth may obscure or simulate indications of neural compromise.<sup>5</sup>

INM is a dynamic process. If electrophysiological data are inadequate, adjustments can be made to the type of modality employed, or the position of electrode placement. Should this be optimised, the anaesthetist may choose to eliminate the inhalational agent, or to use etomidate or ketamine to enhance cortical responses.<sup>5</sup>

## Conclusion

The use of INM has given the surgical team the opportunity to provide a safe and more effective service to the patient, requiring delicate surgery to neuronal structures. The development of an anaesthetic approach which optimally aids the surgeon and neurophysiologist to provide this service remains challenging, and many different protocols exist. From a survey of 25 centres in North America, 35 different protocols for paediatric surgery with INM have been published.<sup>4</sup> This provides a clear indication of the many contentious issues and different approaches that exist for anaesthesia in these patients. As INM is developed

as a modality in South Africa, it is important that the South African Society of Anaesthesiologists provides support to the development of standardised protocols, and acknowledges that adequate training in their application by anaesthesiologists, neurophysiologists and surgeons is essential. Safe and optimal neurological outcome should be the priority for these patients, and anaesthesiologists play a crucial role.

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