University of Groningen

Anesthesia and intraoperative neurophysiological spinal cord monitoring

Sahinovic, Marko M.; Gadella, Maria C.; Shils, Jay; Dulfer, Sebastiaan E.; Drost, Gea

IMPORTANT NOTE: You are advised to consult the publisher's version (publisher's PDF) if you wish to cite from it. Please check the document version below.

Document Version
Publisher's PDF, also known as Version of record

[Link to publication in University of Groningen/UMCG research database](#)

Anesthesia and intraoperative neurophysiological spinal cord monitoring

Marko M. Sahinovic[a], Maria C. Gadella[b], Jay Shils[c], Sebastiaan E. Dulfer[b], and Gea Drost[b,d]

Purpose of review
We will explain the basic principles of intraoperative neurophysiological monitoring (IONM) during spinal surgery. Thereafter we highlight the significant impact that general anesthesia can have on the efficacy of the IONM and provide an overview of the essential pharmacological and physiological factors that need to be optimized to enable IONM. Lastly, we stress the importance of teamwork between the anesthesiologist, the neurophysiologist, and the surgeon to improve clinical outcome after spinal surgery.

Recent findings
In recent years, the use of IONM has increased significantly. It has developed into a mature discipline, enabling neurosurgical procedures of ever-increasing complexity. It is thus of growing importance for the anesthesiologist to appreciate the interplay between IONM and anesthesia and to build up experience working in a team with the neurosurgeon and the neurophysiologist.

Summary
Safety measures, cooperation, careful choice of drugs, titration of drugs, and maintenance of physiological homeostasis are essential for effective IONM.

Keywords
D-waves, intraoperative neurophysiological monitoring, somatosensory evoked potential, total intravenous anesthesia, transcortical electrical stimulation of Motor Evoked Potentials

INTRODUCTION

The goals of intraoperative neurophysiological monitoring (IONM) are to preserve neurologic function during surgery and to help optimize surgical results. In order to identify impending damage to the nervous system before it is irreversible, a set of so-called 'warning criteria' were proposed. These warning criteria can be rightfully triggered by surgical manipulation. However, anesthesia can also significantly impact the efficacy of the neurophysiologic measurements, potentially triggering warning criteria. Furthermore, diverse technical problems can cause changes in these neurophysiological signals. As a result, the efficacy of neurophysiological monitoring depends on good cooperation between the surgeon, anesthesiologist, and clinical neurophysiologist. It is crucial that the anesthesiologist(s) builds up experience with the clinical neurophysiologist and the surgeons so that this 'trinity' forms a team based on mutual trust and good communication. This trust is critical in optimizing the outcome of the procedure when IONM is used [1,2]. Nuwer *et al.* have shown that teams that work together regularly are effective in spinal surgery, whereas inexperienced teams can have worse outcomes than those not using IONM [1].

In this article, we focus on spinal cord monitoring during spinal surgery. We do not go into any detail related to cauda equina and nerve root mapping and monitoring. Subsequently, we review the

[a]Department of Anesthesiology, [b]Department of Neurosurgery, University Medical Center Groningen, University of Groningen, Groningen, The Netherlands, [c]Department of Anesthesiology, Rush University Medical Center, Chicago, Illinois, USA and [d]Department of Neurology, University Medical Center Groningen, University of Groningen, Groningen, The Netherlands

Correspondence to Dr M. Sahinovic, Department of Anesthesiology, University Medical Center Groningen, University of Groningen, Groningen, The Netherlands. Tel: +31503616161;
e-mail: m.sahinovic@umcg.nl

KEY POINTS

- Teamwork, communication, and cooperation are essential for optimal patient management during spinal surgery with intraoperative neurophysiological monitoring.

- Careful choice of drugs, and titration of the drug doses, are necessary to provide optimal conditions for IONM.

- Maintenance of physiological homeostasis is essential to limit the risks of intra-operative hypoxic or ischemic neurological injury and false-positive IONM findings.

- Anesthesiologists should have a preprepared systematic action plan to manage an IONM alert (a) communicate with the neurophysiologist and the surgeon; (b) ensure normothermia, normotension, normoxia and normocapnia, optimal anesthetic depth; (c) replace/switch anesthetic drugs that might potentially be interfering with the IONM; (d) use adjuncts to reduce propofol requirements; (e) discuss a wake-up test or staging/abandon the procedure.

spinal cord monitoring methods employed by the neurophysiologist and their interplay with anesthesia (see Table 1). Further, we provide a roadmap that may be used when possible damage to a neural structure is detected. Finally, we acknowledge the importance of good teamwork.

PREOPERATIVE EVALUATION

Extra attention should be focused on several procedure-specific factors when performing a preoperative evaluation of a patient about to undergo spinal surgery using IONM.

Any existing neurological defects should be documented to facilitate intra- and postoperative surveillance and detection of new injuries. Joints should be tested for their range of motion to identify potential limitations that could impede proper prone positioning.

Further, since propofol is the hypnotic drug of choice when IONM is utilized, contra-indications for its use, such as allergy or mitochondrial disease, should be ruled out.

Lastly, patients must be screened for other (relative or absolute) contraindications for IONM use. These are: loose teeth, epilepsy, pro-convulsant medication, intracranial electrodes, vascular clips, shunts, cardiac pacemakers, or other implanted medical devices.

INTRAOPERATIVE NEUROPHYSIOLOGICAL MONITORING TECHNIQUES

Preservation of the functional integrity of the sensory and motor systems is the most critical goal of intraoperative spinal cord monitoring. IONM uses the following well-known neurophysiological monitoring methods: electroencephalography (EEG), electromyography (EMG), and evoked potentials (EPs).

A well-described technique, in connection with a structure or part of the nervous system to be monitored, is called a modality. Monitoring consists of near-continuous recording, assessing the ongoing functional integrity of at-risk neurological structures or pathways. Almost all monitoring is 'multi-modal', which means that more than one modality is used during surgery.

Somatosensory evoked potentials

The modality used to monitor the sensory tracts of the spinal cord is somatosensory evoked potential (SSEP) monitoring [3]. It was developed in the mid-1970s and was the first neurophysiological technique used for this goal. During spinal surgery, both upper and lower extremity SSEPs are usually monitored. Stimulation of the median or ulnar nerve at the wrist, and stimulation of the tibial nerve, mainly at the ankle, evoke a potential that, after averaging, can be recorded at the scalp. Amplitude declines of 50% and latency changes of more than 10% are common alarm criteria. MacDonald *et al.* also stress the need for adaptive SSEP alarm criteria.

Transcortical electrical stimulation of Motor Evoked Potentials

Transcortical electrical stimulation of Motor Evoked Potentials (Tc-MEPs) provides sensitive and specific information about motor function. After transcortical electrical stimulation, MEPs can be registered directly at the epidural or subdural space of the spinal cord (Direct waves or D-waves). With an adaptation of the stimulus parameters, Tc-MEPs can also be recorded from the muscles (mTc-MEPs).

D-waves are compound motor action potentials initiated by direct axonal activation and are obtained by a single cortical stimulus. If there is an amplitude decline of more than 50% or a total disappearance of the signal, there is a high probability of severe neurological deficit, e.g., permanent paraplegia [4]. An advantage of D-wave monitoring is that the waveform is highly reproducible, and the amplitude can be determined very precisely. It correlates most accurately with long-term motor function in intramedullary spinal cord surgery [5]. A disadvantage of D-waves is that they cannot be recorded reliably beyond the level of 10th–11th thoracic vertebrae since there are insufficient numbers of corticospinal tract fibers below that level.

Table 1. Do's and don'ts during anesthesia for spine surgery using intraoperative neurophysiological monitoring

Do's	Don'ts
Preoperative evaluation	
• Note any neuromuscular or musculoskeletal defects	• Administer excessive premedication
• Ensure no contraindication to propofol	
• Preclude contraindication for IONM ICD, pacemaker, cardiac arrhythmias, intracerebral aneurysm clips or other metals implants, loose teeth, epilepsy:	
Positioning and safety	
• Ensure optimal respiratory tube fixation	
• Ensure optimal prone position	
• Use bite-blocks in case of MEPs	
• Check cable positions and connections	
• Prevent pressure sores caused by IONM wiring	
• Check for electrical interference by using free-running EEG/EMG	
Drugs	
• Use total intravenous anesthesia	• Use volatile anesthetics
• Use target-controlled infusion	• Administer the drug in bolus form
• Make use of hypnotic/opioid interaction and minimize the hypnotic dose	• Use NMB agents intra-operatively
• Optimize/minimize hypnotic dose using depth of anesthesia (DOA) monitor	
• Consider using adjuvant drugs to minimize TIVA dose (e.g., ketamine)	
Physiology	
Maintain:	Avoid:
• Euvolemia	• Hypo/hypertension
• Normotension *(MAP>60 mmHg, adjust according to patient and intraoperative factors)*	• Excessive use of vasopressors
• Normoxia	• Avoid burst-suppression EEG pattern during IONM
• Normocapnia	
• Normal hemoglobin concentration	
Postoperative management	
• Strive for early emergence and extubation	
• Follow the ERAS protocol	

EEG, electroencephalography; EMG, electromyography; ERAS: Enhanced recovery after surgery; ICD: Implantable Cardioverter Defibrillator; IONM, intraoperative neurophysiological monitoring; MAP, mean arterial pressure; MEPs, Motor Evoked Potentials.

In 1980, Merton and Morton described the technique of transcortical electric stimulation in which motor cortex stimulation elicits measurable motor potentials at the muscles [6]. However, this method failed to produce the same results in patients under anesthesia. Later, Taniguchi *et al.* reported that this anesthesia-related signal suppression could be overcome by using short stimulation 'pulse trains' instead of a single pulse to stimulate the motor cortex. [7]. MacDonald *et al.* showed that intraoperative mTc-MEP monitoring is sufficiently safe in the hands of experts when using appropriate precautions for this type of monitoring [8]. Warning criteria of the mTc-MEP depend on the type of surgery performed and can vary between 50% amplitude reduction to the total disappearance of the mTc-MEPs [4]. mTc-MEPs alone do not have high specificity. Losing the mTc-MEP recordings with

preserved D-wave recordings does not necessarily herald irreversible neurological damage but might merely signal transient neurological deficit instead.

There are also other differences between mTc-MEPs and D-wave recordings. Because of the polysynaptic origin of mTc-MEPs, its configuration is polyphasic, more variable and more sensitive to the suppressive effect of anesthetics drugs. This means that amplitude estimation in these recordings is less precise. Furthermore, in contrast to D-waves, mTc-MEPs enable monitoring the whole motor corticospinal tract, from the cerebral cortex to the muscles.

'Free running' electromyography and electroencephalography

Spontaneous electrical signals recorded at the muscles ('free-running EMG') or the scalp ('free-

running EEG') can be continuously registered using IONM equipment.

EMG activity can be used for measurement of the electrode impedance. It can also be used to detect abnormal motor unit activity due to, for example, a radicular nerve lesion.

The free-running EEG provides an insight into the cerebral anesthetic drug effect. This is important since excessive hypnotic drug doses can interfere with the Tc-MEPs, and to a lesser degree, SSEP recordings. Even when total intravenous anesthesia (TIVA) is used, and especially when mTc-MEPs monitoring is used, the goal is to optimize the drug dose in order to avoid burst suppression activity. When burst suppression is present, cortical excitability is significantly reduced, and this will adversely influence the amplitude of the neurophysiological signals recorded.

INTRAOPERATIVE MANAGEMENT

Positioning and safety

Placing the patient in the prone position has a significant influence on cerebral, respiratory and cardiovascular physiology and can lead to considerable morbidity if not executed correctly [9].

The airway device of choice for patients placed in the prone position, is a securely attached endotracheal tube. When Tc-MEP monitoring is used, bite blocks should be placed in the back of the mouth between the molar teeth. The electrical stimuli used to induce mTc-MEPs can cause a masseter muscle contraction leading to a forceful closure of the mouth, potentially causing intraoral injury and endotracheal tube damage.

When a patient is positioned correctly in a proper prone position, pressure should be evenly distributed across their chest and pelvis. The pressure applied on the neck, abdomen, and groin area should be minimized. Compression of the neck can impede the flow through the carotid arteries and jugular vein, compromising cerebral perfusion. Abdominal compression can decrease pulmonary compliance and compress the inferior vena cava, thereby compromising the ventilation and the circulation, whereas compression of the groin area can lead to obstruction of femoral vein and artery, compromising the circulation of the legs [10].

Drugs

Advisable for use during intraoperative neurophysiological monitoring

Hypnotics
Propofol

Propofol is the most suitable hypnotic drug for the maintenance of anesthesia during surgery with IONM. Even though its administration leads to a decrease in amplitude of mTc-MEPs and SSEPs and an increase in latency of SSEPs, when administered in clinically relevant doses, it does not interfere with IONM [11,12]. Nonetheless, it is essential to (a) optimize (minimize) the administered drug dose, (b) maintain a steady hypnotic drug effect, and (c) avoid administering large boluses.

These goals can be best achieved using target-controlled infusions (TCI) and by monitoring the hypnotic drug effect with an EEG-based depth of anesthesia (DOA) monitor.

Propofol administration with a TCI pump enables the user to quickly achieve the desired hypnotic drug effect and maintain steady drug effect levels during prolonged infusion. The pumps are programmed with a pharmacokinetic-pharmacodynamic (PK-PD) model, that is used to calculate the infusion rates necessary to achieve the plasma or effect-site target concentration selected by the user, taking into account different patient characteristics that influence the PKs of propofol [13]. There are multiple propofol PK-PD models available and each has its pros and cons [14]. The Eleveld general-purpose propofol PK-PD model is the most recently developed model, and has the potential to provide accurate propofol TCI administration in a broad population of patients [15].

An EEG-based DOA monitor can assist tailoring the propofol dose (or the target concentration with TCI administration of propofol is used) to the individual patient's needs. These monitors analyze spontaneously generated, processed EEG signals in the frequency, phase and time domains, often using a proprietary algorithm, to quantify the achieved drug effect [16]. Each monitor has limitations, and using it effectively requires experience [17]. It is also advisable that the anesthesiologist not only relies on the indexed output of the monitor, but also observes the raw EEG trace shown on the monitor.

Benzodiazepines

Due to their sedative, amnestic and anxiolytic properties, short-acting benzodiazepines such as midazolam are suitable agents for premedication. Higher doses of benzodiazepines result in a significant reduction in mTc-MEP amplitude and an increase in mapping threshold in a dose-dependent manner. On the other hand, smaller, anxiolytic doses of benzodiazepines exert minimal effects on SSEP and mTc-MEPs and do not impede evoked potential monitoring [11].

Opioids

Opioids, when administered alone, lead only to a small cortical suppressive effect that does not

significantly impact IONM. They remain the cornerstone of balanced anesthesia. Through their intraoperative synergistic interaction with the hypnotic drugs, they exert multiple effects. First, they minimize the adrenergic autonomic responses to surgical stimuli, thereby ensuring intraoperative hemodynamic stability and minimizing perioperative surgical stress response. Furthermore they potentiate the hypnotic drug effect, thereby enabling a reduction of the hypnotic drug dose and attenuating the adverse effects of the hypnotic drug.

Inadvisable for use during intraoperative neurophysiological monitoring

Volatile anesthetic drugs

Inhalational anesthetics cause a significant dose-dependent reduction in the amplitude of SSEPs and mTc-MEPs when used in clinically relevant doses, making them unsuitable as a sole drug for the maintenance of anesthesia during surgery with IONM. The suppressive effect can be partially overcome using higher intensity and multipulse stimulation, but this is increasingly less effective as the drug dose increases beyond a minimal alveolar concentration of 0.5 [18].

Neuromuscular blocking agents

All neuromuscular blocking (NMB) agents impede neuromuscular junction signal transfer, thereby decreasing mTc-MEP amplitude in a dose-dependent manner. Deep neuromuscular block is thus incompatible with mTc-MEP monitoring [19].

NMB, nonetheless, can still play an essential intraoperative role. First, during induction of anesthesia, they facilitate airway management; however, judicious dosing is vital to avoid prolonged drug effect. Further, in some cases the neurophysiologist may request some degree of muscle relaxation to improve SSEP and D-wave monitoring by eliminating spontaneous EMG activity [20].

Physiology

Ensuring optimal oxygen delivery to the spinal cord

Neuronal tissue has high metabolic demands requiring a constant and uninterrupted supply of oxygen for proper functioning (DO2). This goal can be achieved by optimizing blood oxygen transport capacity by ensuring sufficient ventilation and oxygenation, blood oxygen content, and blood flow.

Oxygenation and ventilation

Only extremes of hypo/hyperoxia and hypo/hypercapnia exert a measurable influence on EPs. Mild hypoxemia (down to end-tidal O_2 48 mmHg), and hypocapnia does not affect the SSEP [21]. Severe and persistent hypoxia or hypocapnia (arterial CO_2 <20 mmHg) leads to SSEP latency increases and amplitude decreases [12].

Blood oxygen content

For optimal oxygen tissue delivery, hemoglobin levels must be adequate. Acute decreases in hematocrit below 15% lead to a progressive decrease in amplitude and prolonged latencies in SSEP. This effect can be reversed by blood transfusion to achieve a hematocrit of 22% or more [21]. It is advisable to follow the American Society of Anesthesiologists guidelines for perioperative Blood Transfusion and keep the hemogloblin levels within the recommended range [22].

Blood flow and tissue perfusion of the spinal cord

Blood pressure is a driving force behind spinal cord perfusion. Its effect is modified by the spinal cord autoregulation system, which keeps the blood flow constant in the face of changing perfusion pressure by altering the vascular resistance. It mirrors cerebral autoregulation function, where the stable blood flow is maintained when mean arterial pressure (MAP) is between 50 and 150 mmHg in healthy adults.

Age, preexistent hypertension, and diabetes, as well as local factors such as arterial stenosis or increased tissue pressure, might derange the autoregulation system, thereby increasing the lower limit of the autoregulation, necessitating higher-than-normal blood pressures for adequate perfusion.

It is currently not clear what blood pressure is sufficient to ensure spinal cord perfusion [23▪▪] but decreasing the pressure below this level (of autoregulation) leads to progressive mTc-MEP and SSEP amplitude decreases without affecting latency [21,24]. Adhering to the generally accepted population-based lower and upper MAP threshold of 60–70 mm Hg and 160 mm Hg [25] and adjusting these targets by monitoring the EPs is advisable.

Temperature

Hypothermia decreases axonal conduction velocity thereby increasing the latency of cortical SSEPs and spinal mTc-MEPs. The amplitude of mTc-MEPs decreases, whereas the amplitude of SSEP correlates poorly with temperature. In animal studies, hypothermia has been shown to decrease the sensitivity of IONM for spinal cord injury (more false negatives)

[26]. Hyperthermia has converse effects and reduces latency in all EPs.

The latency change becomes significant at around a 2–2.5 degree change, suggesting that the intraoperative temperature should be maintained between 35 and 37°C [27].

Troubleshooting in response to an intraoperative neurophysiological monitoring alerts

If the IONM 'warning criteria' are met (an IONM event), it is of utmost importance to quickly and efficiently identify and correct the cause. Having a preprepared, systematic action plan can make this task much more manageable. See Table 2 for an example of such a plan.

First, it is essential to determine if the IONM event is reproducible (i.e., not caused by interference or equipment malfunction). If so, the whole team should be alerted to the problem, and surgical manipulation should be halted. Subsequently, the pattern and timing of the signal changes should be determined as these can allude to their cause.

An acute signal alteration caudal to the level of surgical manipulation, with the cranial signals unaffected, strongly suggests a surgical cause of spinal cord injury. This can be caused by direct (mechanical) damage, necessitating reversal of the most recent surgical interventions, or an indirect (ischemic) injury where blood pressure should be augmented to improve the spinal cord perfusion.

A sub-acute global signal change, on the other hand, suggests a systemic or anesthetic problem. In this case, DOA, blood pressure (MAP >60 mm Hg), blood volume, hematocrit (>30%), and temperature (>35°C) should be checked and corrected if needed. It should be determined if the signal change can be attributed to any boluses of drugs, including NMB agents, in which case neuromuscular block must be reversed.

POSTOPERATIVE MANAGEMENT

At the end of the surgery, a rapid return of consciousness and extubation are desirable. An early wake-up allows immediate evaluation of neuromuscular function and rapid detection of early postoperative

Table 2. Systematic action plan for managing an IONM alert

Management guideline IONM warning		
Initial actions		
Check if the IONM warning is reproducible		
Clearly communicate the problem to the whole team		
Pause any further surgical manipulation		
Evaluate the cause		
Anesthetic Systemic	Neuro-physiological Technical	Surgical Mechanical
• Optimize anesthetic depth	• Check electrodes and connections	• Consider irrigating the spinal cord with saline
• Ensure no neuromuscular blocking agents	o Equipment failure or electrical interference?	• Evaluate/undo actions before the signal change:
• Optimize:	o Consider increasing stimulation intensity	o Remove rods/screw
o Oxygenation	• Determine attributes of signal change	o Stop traction
o Ventilation	o Acute/Sub-acute	o Check dura for compression
o Blood volume	o Unilateral/generalized	
o Hematocrit	o Cranial/caudal to the level of the surgical manipulation?	
o Blood pressure	o Repeat MEP measurements	
• Ensure normothermia		
• Consider		
o Hypnotic drug rotation		
o Adding adjuvant drugs (e.g., ketamine)		
Consider		
Consult with a colleague		
Staging/abandoning the surgical procedure		
Performing a Wake-up test		

IONM, intraoperative neurophysiological monitoring; MEP, motor evoked potential.

complications. These benefits should be weighed against the potential benefits of delayed awakening and extubation in some situations such as after extensive blood loss and transfusion or facial swelling in a patient who has been in a prone position for a protracted period of time.

Subsequent recovery should follow the guidelines of enhanced recovery after spine surgery since a recent meta-analysis [28] suggests that this may reduce postoperative complication rates, readmissions, length of stay, and opioid use, whereas it improves postoperative functional outcome of surgery.

CONCLUSION

With an ever-growing complexity of spinal surgery performed in patients with increasing neuro-pathology, age, and co-morbidity, there is a need for a quick, accurate, and reliable way to monitor critical structures of the nervous system. IONM provides this. However, its efficacy is dependent on the collaboration of all personnel involved. In a complex intraoperative environment teamwork, trust, and communication between the surgeon, the neurophysiologist, and the anesthesiologist are essential.

This manuscript summarizes the IONM principles and their interplay with anesthesia and provides an IONM troubleshooting guide. It encourages communication, mutual understanding, and cooperation during surgery, as this improves surgical outcomes for the patient.

Conflicts of interest
M.M.S. reported no conflicts of interest.
M.C.G. reported no conflicts of interest.
J.S. is a Consultant at Medtronic, and Author for Elsevier.
S.E.D. reported no conflicts of interest.
G.D. reported no conflicts of interest.

REFERENCES AND RECOMMENDED READING
Papers of particular interest, published within the annual period of review, have been highlighted as:
- ■ of special interest
- ■■ of outstanding interest

1. Nuwer JM, Nuwer MR. Neurophysiologic surgical monitoring staffing patterns in the USA. Electroencephalogr Clin Neurophysiol 1997; 103:616–620.

2. ElBardissi AW, Sundt TM. Human factors and operating room safety. Surg Clin N Am 2012; 92:21–35.
3. MacDonald DB, Dong C, Quatrale R, *et al.* Recommendations of the International Society of Intraoperative Neurophysiology for intraoperative somatosensory evoked potentials. Clin Neurophysiol 2019; 130:161–179.
4. MacDonald DB. Overview on criteria for MEP monitoring. J Clin Neurophysiol 2017; 34:4–11.
5. Morota N, Deletis V, Constantini S, *et al.* The role of motor evoked potentials during surgery for intramedullary spinal cord tumors. Neurosurgery 1997; 41:1327–1336.
6. Merton PA, Morton HB. Stimulation of the cerebral cortex in the intact human subject. Nature 1980; 285:227.
7. Taniguchi M, Cedzich C, Taniguchi M, *et al.* Modification of cortical stimulation for motor evoked potentials under general anesthesia: Technical description. Neurosurgery 1993; 32:219–226.
8. MacDonald DB, Skinner S, Shils J, Yingling C. Intraoperative motor evoked potential monitoring – a position statement by the American Society of Neurophysiological Monitoring. Clin Neurophysiol 2013; 124:2291–2316.
9. Kwee MM, Ho Y-H, Rozen WM. The prone position during surgery and its complications: a systematic review and evidence-based guidelines. Int Surg 2015; 100:292–303.
10. Feix B, Sturgess J. Anaesthesia in the prone position. Contin Educ Anaesth Crit Care Pain 2014; 14:291–297.
11. Dineen J, Simon MV, Ala N. Anesthesia and intraoperative neurophysiology. New York, NY: Springer Publishing Company; 2018.
12. Sloan TB, Heyer EJ. Anesthesia for intraoperative neurophysiologic monitoring of the spinal cord. J Clin Neurophysiol 2002; 19:430–443.
13. Sahinovic MM, Absalom AR, Struys MM. Administration and monitoring of intravenous anesthetics. Curr Opin Anaesthesiol 2010; 23:734–740.
14. Sahinovic MM, Struys MMRF, Absalom AR. Clinical pharmacokinetics and pharmacodynamics of propofol. Clin Pharmacokinet 2018; 57:1539–1558.
15. Eleveld DJ, Colin P, Absalom AR, Struys MMRF. Pharmacokinetic–pharmacodynamic model for propofol for broad application in anaesthesia and sedation. Br J Anaesth 2018; 120:942–959.
16. Fahy BG, Chau DF. The technology of processed electroencephalogram monitoring devices for assessment of depth of anesthesia. Anesth Analg 2018; 126:111–117.
17. Palanca BJ, Mashour GA, Avidan MS. Processed electroencephalogram in depth of anesthesia monitoring. Curr Opin Anaesthesiol 2009; 22:553–559.
18. Lotto ML, Banoub M, Schubert A. Effects of anesthetic agents and physiologic changes on intraoperative motor evoked potentials. J Neurosurg Anesthesiol 2004; 16:32–42.
19. Nunes RR, Bersot CDA, Garritano JG. Intraoperative neurophysiological monitoring in neuroanesthesia. Curr Opin Anaesthesiol 2018; 31:532–538.
20. Rabai F, Mohamed B, Seubert CN. Optimizing intraoperative neuromonitoring: anesthetic considerations. Curr Anesthesiol Rep 2018; 8:306–317.
21. Banoub M, Tetzlaff JE, Schubert A. Pharmacologic and physiologic influences affecting sensory evoked potentials. Anesthesiology 2003; 99:716–737.
22. Khanna P, Bhatt R. Practice Guidelines for Perioperative Blood Transfusion and Adjuvant Therapies. Anesthesiology 2006; 105:198–208.
23. Dulfer SE, Sahinovic MM, Lange F, *et al.* The influence of depth of anesthesia
■■ and blood pressure on muscle recorded motor evoked potentials in spinal surgery. A prospective observational study protocol. J Clin Monit Comput 2021.
This is the study protocol of an ongoing study that is investigating the impact of intraoperative blood pressure management and hypnotic drug dose on IONM
24. Fehlings MG, Tator CH, Linden RD. The relationships among the severity of spinal cord injury, motor and somatosensory evoked potentials and spinal cord blood flow. Electroencephalogr Clin Neurophysiol Potentials Sect 1989; 74:241–259.
25. Sessler DI, Bloomstone JA, Aronson S, *et al.* Perioperative Quality Initiative consensus statement on intraoperative blood pressure, risk and outcomes for elective surgery. Br J Anaesth 2019; 122:563–574.
26. Seyal M, Mull B. Mechanisms of signal change during intraoperative somatosensory evoked potential monitoring of the spinal cord. J Clin Neurophysiol 2002; 19:409–415.
27. Oro J, Haghighi SS. Effects of altering core body temperature on somatosensory and motor evoked potentials in rats. Spine 1992; 17:498–503.
28. Elsarrag M, Soldozy S, Patel P, *et al.* Enhanced recovery after spine surgery: a systematic review. Neurosurg Focus 2019; 46:E3.